DEC 26 1919

ISSUED BI-MONTHLY. VOL. XLVIII., No. 6

ARCHIVES

OF

OPHTHALMOLOGY

FOUNDED IN 1869 BY

DR. HERMAN KNAPP

EDITED IN ENGLISH AND GERMAN

BY

DR. ARNOLD KNAPP
OF NEW YORK
AND
DR. C. HESS
OF MUNICH
AND
DR. W. A. HOLDEN
OF NEW YORK

NOVEMBER

NEW YORK
G. P. PUTNAM'S SONS, 2, 4, & 6 WEST 45TH STREET
AND NEW ROCHELLE, N. Y.
LONDON: 24 BEDFORD STREET, STRAND
WIESBADEN: J. F. BERGMANN'S Verlag
PARIS: J. B. BAILLIÈRE, 19 Rue Hautefeuille
1919
Entered at the Post-Office, New Rochelle, N. Y., as Second-Class Mail Matter

NOTICE TO CONTRIBUTORS.

The editors and publishers of the ARCHIVES beg to offer some suggestions to authors who propose to favor them with the publication of their contributions.

1. Authors will receive gratuitously twenty-five reprints of their articles. If a greater number is desired,—notice of which should be given at the head of the manuscript, or at the latest on the first proof,—only the additional cost of press-work and paper will be charged to the author. The number so ordered should be inclusive of the gratuitous copies.

2. In preparing manuscript for the compositor it is requested that the following rules be adhered to:

a. Write on one side of the paper. Type-written MS. is preferred.

b. Write without breaks, *i. e.*, do not begin each sentence on a new line. When you want to begin a new line or paragraph at a given word, place before it in your MS. the sign ¶.

c. Draw a line along the margin of such paragraphs as should be printed in smaller type—for instance, all that is clinical history in reports of cases, etc.

d. Words to be printed in *italics* should be underscored once, in SMALL CAPITALS twice, in LARGE CAPITALS three times; antique type should be so marked.

e. Let the title of your paper indicate its contents. If it is a general title, for instance, Clinical Contributions, mention the subject of each special communication,—for instance: CASE I. Sarcoma of Iris; CASE II. Exostosis of Frontal Sinus, etc. These special titles will appear in the table of contents of each number and each volume, under the heading of the general title, so that they will not be overlooked.

f. Illustrations should be carefully drawn on separate sheets.

3. Authors receive proofs for revision, which they should correct and return without delay. We beg, however, to remind our contributors that changes in the copy are equivalent to resetting, causing so much additional expense. We therefore request them to make, if possible, no alterations at all in their MSS., or, at least, to limit them to what is of essential importance.

When sending manuscripts for the ARCHIVES OF OPHTHALMOLOGY, please address the editor, Dr. ARNOLD KNAPP, 10 East 54th St., New York City.

CONTENTS OF VOLUME XLVIII., NUMBER 6.

PAGE

1. **Non-Operable Tumor of the Orbit and Brow, Treated Successfully with Radium. Report of a Case with a Few Remarks.** By GEORGE HUSTON BELL, M.D., and SINCLAIR TOUSEY, M.D., New York. (With six illustrations on Text-Plate XVIII.) . 531

2. **Some Cases of Lethargic Encephalitis.** By HIRAM WOODS, M.D., Baltimore, Md. 536

3. **Ocular Complications Due to Typhoid Inoculations.** By F. PHINIZY CALHOUN, M.D. (Atlanta, Ga.,) Major, M. C., General Hospital No. 6, Fort McPherson, Ga. 553

4. **Subretinal Exudate Simulating Sarcoma of the Choroid with Anatomic Examination.** By Dr. ARNOLD KNAPP, New York. (With one illustration on Text-Plate XIX.) 559

5. **Two C[illegible] of Epithelioma of the Eyeball and Lids. Operation. No Return after Eleven and Six Years.** By DUNBAR ROY, M.D., Atlanta 563

6. **A Positive Focal Tuberculin Reaction in a Spindle Cell Sarcoma which had Perforated the Sclera.** By J. W. CHARLES, M.D., St. Louis 568

7. **Persistent Posterior Fibrovascular Sheath of the Lens. A Report of Two Clinical Cases and Three Eyeballs Examined Microscopically.** By Dr. FRANCIS LANE, Chicago. (With fifteen illustrations on Text-Plates XX.–XXII.) 572

8. **Antidiphtheritic Serum in Severe Ocular Infections with Special Reference to Hypopyon Keratitis.** By Dr. BEN WITT KEY, New York 581

9. **Report on the Teaching and Examination of Medical Students in Ophthalmology** 614

10. **Report of the Annual Congress of the Ophthalmological Society of the United Kingdom.** By Mr. H. DICKINSON, London. (*Concluded from the September number.*) 625

PAGE

11. **Book Notice** 632
VII.—Manual of Neuro-Surgery.

12. **Index of Authors and Subjects, Volume XLVIII** . . . 633

VOL. XLVIII. No. 6.

ARCHIVES OF OPHTHALMOLOGY.

NON-OPERABLE TUMOR OF THE ORBIT AND BROW, TREATED SUCCESSFULLY WITH RADIUM. REPORT OF A CASE WITH A FEW REMARKS.[1]

BY GEORGE HUSTON BELL, M.D., AND SINCLAIR TOUSEY, M.D., (BY INVITATION), NEW YORK.

(With six illustrations on Text-Plate XVIII.)

SKEPTICISM in regard to the value of radium in the treatment of malignant and non-malignant tumors is fast disappearing. It is now generally recognized by surgeons of the largest clinics that radium is a great therapeutic agent and a valuable adjunct in the treatment of cancerous and precancerous growths. For these reasons we decided to try radium with this patient.

A woman, aged 65 years, came to Dr. Bell's clinic at the New York Eye and Ear Infirmary on December 13, 1917, with the following history: nine months before she ran into a door jamb and struck her forehead a severe blow on the left side.

The first thing she noticed was a lump on her forehead, which at times gave her some pain. She went to Bellevue Hospital, where she was treated in the Out-Patient Department for six months, with anti-syphilitic treatment, although her Wassermann at that time was negative.

After the swelling on the forehead became more noticeable, she observed that her left eye began to get more prominent than the other one, and the upper lid began to swell. The tumor got larger and larger, the eye more prominent, and the pain increased. Finally she was sent to the New York Eye and Ear Infirmary for treatment.

Status Præsens. Her whole head and face was enveloped in a black veil; on removing it, she presented a ghastly

[1] Read at meeting of American Ophthalmological Society, Atlantic City, June, 1919.

spectacle. Under the bandage which was soaked with blood was an enormous tumor of the orbit and brow. The cornea had ulcerated and perforated, and the eye was bleeding freely. The globe was markedly proptosed. The tumor had pushed out of the orbit, the eyeball, which was displaced downward and inward. There was a solid tumor filling the orbit, which extended well over onto the frontal bone. The upper lid was greatly swollen, and the tension was so great that it could not be elevated. The eyebrow and the skin of the forehead were greatly stretched. The cornea could be seen projecting between the eyelids. See photograph No. 1. This was taken on her first visit to the hospital and will give you some idea of the growth.

The patient was ordered into the hospital at once. She was so weak that we did not try to get a section of the growth for the laboratory.

An X-ray of the skull, including the teeth, was ordered, also a Wassermann.

Previous history: Married and four children, all of whom are living. Had not been sick in twenty years. Had never had a miscarriage. The last sickness that she remembers having was typhoid fever.

Dr. Dixon's report of X-ray findings of skull: Frontals about proper size; right fairly clear; left rather hazy, due to overlying tumor. Left orbit seemed filled with the growth, and there was a soft-looking area in the frontal bone above the left orbit. Antra were fairly clear. Sphenoids were large and did not seem to be involved.

X-ray of teeth: considerable amount of alveolar absorption with what appears to be a cavity around the almost completely absorbed roots of the upper bicuspids, and some absorption at the roots of the molars.

On inspection of the mouth we could see that her gums were not pink, firm, and healthy-looking, but were purplish and swollen and there was a red line adjacent to the teeth. We decided that she had a dirty mouth and we had all her teeth (12) extracted. The report on her Wassermann was negative. This was the second negative report.

The patient was shown by Dr. Bell at a meeting of the New York Ophthalmological Society, and also at the Section of Ophthalmology at the New York Academy of Medicine. All the oculists who saw her advised against an operation. It was then that we decided to use radium, and Dr. Tousey very kindly offered to treat the patient, and to use his radium salt. The first treatment, which lasted one hour, was given on December 19, 1917.

Applications were made of 20 milligrammes of radium salt of two million activity. This was enclosed in a sealed glass

tube, that again in an aluminum treatment tube, that in a lead wrapping about $\frac{1}{60}$ inch thick, and that finally in the soft rubber cover from Oberlander's urethrometer. The radium was left in one place for an hour at each treatment. The places were 1½ inches apart and at first the tumor was so large that there were six of these areas to be treated, one each week. Two weeks from the first treatment decided shriveling of the skin was to be noted, and the patient was sure the tumor was smaller. The surface was of less and less extent so that toward the end only two places received the application, one above and one below the supraorbital margin. At no time was there any cutaneous reaction but on the contrary a steady change from the original glistening appearance to that of healthy skin. The first treatment was on December 19th, and the last on April 1st.

The treatments were continued every week by Dr. Tousey, and on March 13th, the second photograph was taken. The improvement was so great, and the reduction in the size of the tumor was so progressive, that we were encouraged to go forward with the treatment. Fig. 2 shows that the teeth had all been pulled.

On April 1st, Dr. Tousey pronounced her cured. There was a shrunken globe remaining, which was enucleated under local anæsthesia.

The last photograph (Fig. 3) was taken May 4, 1918, after the glass eye had been inserted.

Dr. Bell saw the patient again on January 1, 1919. She had had no recurrence of the growth and had gained twenty pounds in weight. This patient had no internal treatment.

The cosmetic result is now about perfect (Fig. 3). The clinical diagnosis of sarcoma was made by us. We are sorry that we have no laboratory report to offer; the patient was so weak and feeble when first seen by us, that we did not feel like torturing her any more. However, we feel confident about the diagnosis.

Zinzi (1), of London, reports a case of orbital sarcoma successfully treated by radium, which had recurred twice, once after enucleation and again after a growth in the orbit had been removed. One hundred and fifty milligrams of radium bromide were used at first, and then two hundred milligrams. Zinzi was so well pleased with this result that he showed the patient on May 5, 1916, before the Ophthalmological Society of the United Kingdom.

Aikins (2), in reviewing radium as a therapeutic agent, speaks

of its great value in rodent ulcers, vernal catarrh, and exophthalmic goiter.

Some of the most careful work has been done by Axenfeld (3). He reported, in 1915, results obtained after treatment by radium, of a case of glioma in a child whose right eye had been removed for glioma. At the time of enucleation of the gliomatous eye, three foci of growth, one rather large, were seen in the left eye. Radium treatment was instituted. He made eleven careful fundus examinations, noting the decrease of the growth, and in eighteen months after the first treatment, reported that one area had disappeared, another was almost gone, and the third, the largest one had very much decreased in size. In 1916 he reported further progress in this case. The largest growth had completely disappeared, leaving only an evidently dead preretinal trace, with no recurrences elsewhere. Axenfeld was able to demonstrate to his own satisfaction the good effects of radium in the treatment of the glioma case.

In conclusion Axenfeld holds that blind gliomatous eyes should be excised, but that for commencing glioma in the still seeing eye, radium is not only justifiable, but obligatory.

C. F. Clark (4) treated sarcoma of orbit by inserting a tube of radium in the orbit after canthotomy and division of external rectus. The radium was left in four hours, and this was repeated every two weeks. The proptosis quickly receded, and in two years the case was apparently cured. It is interesting to note that a nuclear cataract developed after six months of the treatment, perhaps due to the radium.

Recently S. Gifford (5) reports a case of leucosarcoma of the iris, treated by radium. He concludes by saying that in tumors of the iris, treatment by radium should be seriously considered where the growth is not especially rapid. Even if it has reached the iris root, such treatment should be offered to the patient as an alternative to operation, he being observed carefully during each treatment. Where operation is refused, it would seem only just to the patient, to very urgently advise radium.

Henckel (6) reported a case of melanosarcoma of the orbit, treated with radium, which was held in abeyance for two and a half years.

ILLUSTRATING DR. BELL'S AND DR. TOUSEY'S ARTICLE ON "NON-OPERABLE TUMOR OF THE ORBIT AND BROW, TREATED SUCCESSFULLY WITH RADIUM."

FIG. 1.
Taken December 14, 1917.

FIG. 2.
Taken March 13, 1918.
Note the marked reduction in size of tumor, also expression of face since extraction of all the teeth.

FIG. 3.
Taken May 4, 1918, six months after treatment was instituted.
Cosmic result now about perfect.

We have treated five cases of vernal catarrh with radium, the plaques have completely disappeared, leaving no scars at all, and so far there has been no recurrence, after two and three years.

CONCLUSIONS.

We cannot lay too much stress upon the use of radium in all tumors of the eyelids, orbit, and brow, when syphilis can be excluded, and we hold that it should be given a thorough trial by competent observers, before resorting to surgery.

We also feel that radium should be used in tumors of the iris, when syphilis and tuberculosis can be excluded, before resorting to surgery. Most especially do we recommend the use of radium in these iris tumors where they are growing slowly, and where we can keep a close observation of the patient. In the treatment of all intraocular tumors, radium should be seriously considered.

We are of the opinion that radium is the most effective agent we have in the treatment of epithelioma of the eyelids, as it is easily controlled as to dosage and effect.

We look upon radium as a specific in spring catarrh.

We hold and claim that radium has great value as a therapeutic agent, but before instituting treatment in any given case we claim that all the sources of focal infections must be cleared up and eliminated. The established value of radium we think is now pretty well recognized, although it is not used by ophthalmic surgeons as often as one would suppose.

BIBLIOGRAPHY.

1. ZINZI, N. S., London. "Recurrence of Orbital Sarcoma Successfully Treated by Radium." *The Ophthalmoscope*, August, 1916, p. 420.

2. AIKINS, W. H. B., Toronto. "The Established Value of Radium as a Therapeutic Agent." *Canada Lancet*, July, 1917, p. 445.

3. AXENFELD. "Glioma Retinæ and Intraocular Radiotherapy." *Klin. Monat. f. Augenheilk.*, August, 1915, liv., p. 61.

4. CLARK, C. F. "Successful Treatment of Sarcoma of the Orbit." Rev. in *Ophthalmology*, 1914, p. 6.

5. SANFORD, GIFFORD. "Case of Leucosarcoma of the Iris Treated with Radium." *Arch. of Ophth.*, vol. xlvii., No. 3, 1918, p. 241.

6. HENCKEL, E. B. "Report of a Case of Melanosarcoma of the Orbit Treated with Radium." *Amer. Ophthal.*, 1916, p. 560.

SOME CASES OF LETHARGIC ENCEPHALITIS.[1]

By HIRAM WOODS, M.D., Baltimore, Md.

SINCE the early part of 1918, a peculiar disease termed "lethargic encephalitis" has been appearing sporadically throughout Europe, and more recently in America. Because of the frequency with which paralysis of the eye muscles occurs, the disease was at first termed "lethargic ophthalmoplegia." The muscular abnormalities are peculiar: the usual causes of paralysis (syphilis, diabetes, and tabes) are absent. Without actual paralysis, there is often a nystagmoid action of the ocular muscles. There is a tendency to spontaneous recovery.

Insomuch as the ocular manifestations do not seem to have been heretofore made the object of special study, it has seemed worth while to report somewhat minutely several cases which I had the privilege of observing during the months of February, March, April, and May. In the seven cases, the diagnosis of lethargic encephalitis seemed justified, although in one case (7) it seemed, in the end, erroneous.

HISTORICAL.

The disease appeared first during the winter of 1916–17 in Vienna and was termed "encephalitis lethargica" by von Ecnomo (1). In March, 1918, Netter (2) at the Société Médicale des Hôpitaux at Paris drew attention to several cases of lethargic encephalitis which were occurring sporadically throughout Paris. In the April following, in England, seven cases were reported by Harris (3), and ten by Hall (4) who at this time were inclined to believe the disease due to an infection

[1] Read at meeting of the American Ophthalmological Society, Atlantic City, June, 1919.

by bacillus Botulinus from ingestion of contaminated food. This assumption was, however, immediately questioned by McCaw, Perdrau, and Stebbing (5) and still later by Melland (6). Meanwhile many additional cases were reported. On May 5th, at the Academy of Medicine of Paris, Netter (7) again reported upon cases which were appearing in increasing numbers. At this time Netter drew attention to the similarity of this outbreak with the epidemic of Nona, which in the spring of 1890 followed the pandemic of influenza. Throughout 1918 cases continued to occur in France and England, causing such concern in England that it was made the subject of an extended investigation by the Local Government Board, through their Medical Research Committee.

In this country the disease seems to have appeared early in 1919. On February 21st, at the Institute of Medicine of Chicago, during the discussion on influenza, Dr. Peter Bassoe (8) reported having seen several cases in Chicago. Lethargic encephalitis was the subject of editorial comment in the *Journal of the American Medical Association* in February, 1919, and again in March, while cases were reported by Ely (9) in April and by Tucker (10) in May.

The symptoms of the disease as described by the above authors consist in a rather insidious onset, the patient becoming languid and drowsy with or without headache and vomiting. This drowsiness gradually deepens into a profound stupor. This stupor may last for days or weeks. Almost as common as the sleep are the muscular and nervous phenomena. These usually point to an involvement of the bulbo-pontine area and consist of ophthalmoplegias of various extent, usually extrinsic (ptosis, recti muscles), more rarely intrinsic. Common paralyses, also, are those of the facial nerves, of speech and deglutition. More exceptionally general muscular tremors are observed and but rarely is there paralysis of the limbs. Melland (6) states the case as follows: "Special symptoms produced by the disease depend, of course, upon the particular region of the gray matter of the brain involved. For example, polioencephalitis superior, which affects the nuclei of the cerebrum and cerebellum, may give rise to marked mental changes, coma, hemiplegia, diplegia, and ataxia; while polioencephalitis inferior, which affects the nuclei of the pons and medulla, may

cause paralysis of one or other or several of the cranial nerves, and combination of the two may be met with."

Fever is usually present but not always and is not of long duration. When present it simulates the temperature chart of typhoid fever. Kernig's sign is rarely present. The examination of the cerebrospinal fluid shows only slightly abnormal findings. The tension is usually normal or only slightly raised. Globulin and glucose are usually not present. The cell count in not generally greatly elevated, and when increased, the increase is in lymphocytes. Indeed, Netter considers the relatively normal appearance of the spinal fluid to be of great aid in the diagnosis.

The course of the disease is variable, running from several days to several weeks or even months, and terminates usually in complete cure or in death without farther bulbar phenomena. In favorable cases the change for the better usually comes sharply; but psychic and somatic changes may persist for some time—difficulty in accommodation being one of the most persistent symptoms. The mortality appears to be about 50% (Netter). Others put it at a lower figure.

The pathology of the disease is obscure. The macroscopic findings reported by various authors are slight, and consist generally in meningeal congestion, petechial hemorrhages throughout the gray and white matter, and in one case œdema and congestion in the floor of the fourth ventricle.

Microscopic examination shows brain lesions somewhat similar to those occurring in the cord in poliomyelitis. These lesions consist of a perivascular cellular infiltration, especially in the bulbo-pontine region and around the nuclei. In the cases showing the symptoms of polioencephalitis superior, the lesions are correspondingly higher up in the cerebrum.

As to etiology, in England it was first thought to be a cerebral toxæmia due to bacillus botulinus, but more prolonged observations and bacteriologic examinations (11) showed this to be erroneous. Likewise, pathologic, bacteriologic, and animal experimentation showed the disease to be distinct from anterior poliomyelitis. Netter reports that von Weisner (11) claims to have reproduced the disease in monkeys by the intradural inoculation of brain emulsion from a patient dead of the disease, but was unable to reproduce the disease if the

brain emulsion was passed through a porcelain filter, showing it was not due to a filterable virus. von Weisner further claimed to have isolated a Gram-positive coccus from the brains of subjects and monkeys who have succumbed to the disease. These findings were not, however, substantiated by bacteriologic researches and animal experimentation of the English investigators, their researches giving negative results (12).

Several observers, notably Bassoe and Tucker, in this country have emphasized the occurrence of this disease following influenza and regard it as a cerebral manifestation of the disease. The English investigators, however, suggest that lethargic encephalitis is an autonomous infection and until conclusive proof can be brought forward proving to the contrary, the disease must be regarded as a "malady sui generis," of which the specific causative agent has not yet been discovered.

CASES SEEN BY THE WRITER.

CASE 1.—*Synopsis.* Referred by Dr. Wm. G. Coppage of Baltimore. Exposure to influenza and diphtheria. Lethargy ten days, diplopia due to paralysis of inferior recti; also anisocoria, cycloplegia, partial ptosis, variation in degree of paralysis, nystagmoid movements, optic neuritis. Condition about four months after onset: defective action in inferior recti and accommodation, normal central vision, field contraction (a late development).

M. N., age 13 years, came to my office, February 18, 1919. He gave this history: well, up to ten days ago; in January was exposed to influenza, but did not have it; two children in the family had diphtheria; patient had had no symptoms of disease, and there had been several cultures taken from his throat, all negative. On February 9th, he visited Camp Meade and on returning home had diplopia and eye pains. Drowsy for ten days before I saw him.

I found him sound asleep in the waiting room; he roused easily, walked into the office and sank instantly into a stupor. Temperature 98°, pulse 42. He was mentally clear when awake. Could open eyes widely but lids drooped and presented appearance of moderate double ptosis. Left pupil larger, doubtful light reaction left, very slight, right. No convergence contraction.

Extrinsic Muscles. Lateral movements normal both ways,

with slight rotary nystagmus at extreme end, each direction. Made no effort at convergence until the test object was within 8 or 10*cm* from eyes. Then he used left lateral motion, fixing with right, the left eye suddenly diverging. Up motions normal; down, entirely lost, both eyes. Orientation defective in all fields except above. Accommodation lost but he read at 33*cm* with + 3.5 d., either eye. Vision right $\frac{18}{18}$, left $\frac{18}{18}$ (–).

Ophthalmoscope showed blurred neuroretinal margins and engorged veins, judged by comparison with size of arteries. Fields were impossible, until the 11th of March (three weeks later) when they were normal. At his first visit, I was inclined to the diagnosis of brain tumor on account of the low neuritis, slow pulse, and stupor; but the character of paralysis, absence of nausea, and history of exposure to infection made this diagnosis very uncertain.

The boy was seen at his home the next day, February 19th, with Dr. M. H. Thomas. In addition to the above, we noted weakness of both facials, Kernig's sign, slight stiffness of neck and tenderness over masseters; patella reflex was exaggerated, other deep reflexes normal. Boy could be made to walk, but gait was unsteady and he would sink into a chair or on a bed and fall into stupor if left alone.

He was sent to the Union Protestant Infirmary for study. Condition continued as stated for three days, when lethargy lightened. He was in hospital to 5th of March (12 days). During that time he presented a variation of symptoms. At times the pupils responded to light almost normally. Then, after a few hours, they would dilate ad maximum and become immobile. No accommodation. The pupils stayed unequal, the left always larger than right. Twice the left pupil changed its shape from regular, full dilation to an oval, with long diameter horizontal. There was similar variation in the deep reflexes. One day all were lost except the left knee. Then they returned. Abdominal reflexes were absent for several days. Dermatographia was constantly present. He voided urine involuntarily. At times the body muscles twitched spasmodically. Kernig's sign persisted. It was always more painful on the left side. The weakness of the facials, noticed on the 19th of February, developed into an almost complete double paralysis and then cleared. Temperature varied from 99 to 101 for three days, then became normal.

Laboratory findings were: urine normal, blood and spinal fluid Wassermann, negative to all tests, the fluid coming under normal pressure, drop by drop and clear. Cell count, 39 to cubic *mm* slightly positive globulin, no organisms. Leucocytosis 7000. After a week in the hospital with these

varying symptoms the lethargy passed off and the boy lay in bed awake, rational. He left the hospital with all symptoms improved except the low grade of optic neuritis, complete paralysis of accommodation, and inferior recti and slight left facial; also unequal pupils, with slight light, and no convergent response.

March 11th (six days later) I found the following: vision, right $\frac{20}{60}$, left $\frac{20}{40}$. The papillitis had about disappeared. Left pupil the larger of two. Good light, slight convergence, reaction: no accommodation. Changing position of eyes from above to the horizontal plane, or lateral movements produced rotatory nystagmus. Eleven days later he showed a little motion down, 15° to 20° on perimeter. Vision was $\frac{20}{40}$ right, and $\frac{20}{30}$ left. Pupillary reaction was good for light and convergence which had completely recovered. Accommodation had improved about one diopter. From this time, there was improvement with, however, occasional variations. These affected vision and mobility. Vision varied from $\frac{20}{30}$ each on March 22d to $\frac{20}{50}$ on the 27th. On the latter day all the gain in accommodation had been lost. On April 17th (two months after onset) vision reached $\frac{20}{15}$. There was no accommodation, + 3.5 sph. being again needed for reading at 33*cm.* This held ten days later. The left pupil remained the larger, but each showed normal reaction. His down movement had increased on April 26th. At the termination of both up and down movements, there was a tremor of the eyes before they became quiet. This was not the case with lateral movements. Accommodation was still nil. Vision was $\frac{20}{15}$ each.

May 26th (five and a half weeks later), his condition was: right vision $\frac{20}{15}$. Read newspaper print for a moment at 40*cm* with the right eye, but could not hold it. Accommodation about two diopters. Vision, left $\frac{20}{15}$. Accommodation one diopter. All movements normal except downwards. Slight nystagmoid movements at end of excursions, up, down, or lateral. Fields show contraction, in comparison with those of six weeks ago. General demeanor heavy and he tires quickly on keeping eyes fixed. Fields, unreliable.

CASE 2.—*Synopsis.* Previous influenza, lethargy followed by "jerking of eyes and difficulty in locating objects till the eyes get still" (patient's description). Nystagmoid movements; facial paralysis.

Mr. N. W., 29 years of age, farmer, saw me first on March 4, 1919. He had a myopia of 1.25 diopters with normal vision. History of influenza the first week in January: recovered. On February 20th, at the automobile show, he

fell asleep. His wife woke him, he walked around a few minutes and went to sleep again. Went home and slept three days and nights. Felt well, but could not keep awake. On February 24th was giddy. Still occasionally so. First eye symptoms on the 25th. He said: "Lids and eyes twitched if I looked at anything; end of last week, eyes did not keep still long enough to pick out print to read."

Examination showed normal fundus and media; vision with glasses right $\frac{20}{15}$, left $\frac{20}{15}$. The right obtained $\frac{20}{15}$ when "it got quiet." Punctum proximum accommodation, five diopters each. Pupillary reflexes and convergence normal. Fixation at any point, distant or near, was followed by a rotatory and sometimes vertical nystagmus which lasted about three seconds. Then eyes became quiet. As soon as the position of the eyes was changed and a new point of fixation sought, oscillations were renewed. When the eyes were closed there were tremor of both upper lids and occasional orbicularis twitching. This was also noted in lateral movements either to the right or left. This condition was observed for three days.

Two days later (March 9th), he developed a most curious muscular action. Convergence and lateral movements were normal, save for the oscillations which passed off in a few seconds. The same was true when he looked downward; but on looking up, following a finger or test object, the eyes moved slowly up, a certain distance, and then, as though working on a spring, they both converged violently. This spasmodic convergence was accompanied by farther jerkings inward. He was totally unable to abduct the eyes when directed above the horizontal plane, but when he was told to look down, the axes became parallel.

On March 11th, he developed right facial paralysis. He said the drawing of the face to the right was a "queer trick," he had. On the 12th, I asked Dr. Thomas to see him with me. All reflexes were normal. Sometimes the hands trembled, also neck muscles. On getting up from a chair the thigh muscles went into a quick irregular tremor lasting a few seconds. After that he walked normally. It was impossible to get the patient to the hospital for laboratory study. After nearly three months his condition is as follows: May 10th, oscillations of eyes slight, but definite. On May 23d my case notes read: "(1) In up motions, left eye lags a little behind the right, but, on urging, the left eye is pulled up as far as right. (2) In fixation on horizontal plane, a tiny rim of left sclera above the cornea is visible; none in right eye. (3) In motions up, slight rotatory nystagmus, sometimes two or three jerks, then eyes are kept still. Face is a little drawn to the left (opposite of condition ob-

served, 11th March.) Pupils, accommodation, convergence, fundus, and media normal." He can read and says he knows he is better because his horse "does not seem to fly about when he is getting into saddle."

CASE 3.—*Synopsis.* Exposure to influenza, had "cold." Headache (only case with this), lethargy, occasional nystagmoid movements.

E. S., boy 14 years of age, consulted me February 18th, for headache and drowsiness. The pain had come first about two weeks previous, slept all the time since. He had been exposed to influenza, but did not think he had had more than a "heavy cold" in December. Still weak.

I found drooping of both upper lids. His vision was $\frac{20}{20}$ and accommodation seven diopters, each eye.

Manifest refraction error, right +1.sph. = −0.37 cyl. ax. 180°
left +1.5 sph. = −0.37 cyl. ax. 180°

Fundus and media normal. The only defect found in motions was in lateral fixation. For instance, in indirect ophthalmoscopic examination—the eyes would suddenly roll up and the upper lids droop. The boy said the eyes did not hurt and he did not know why he could not keep them open. He was so drowsy I could hardly keep him awake long enough to examine the eyes. Lateral fixation either way produced nystagmoid movements.

Under date of March 7th, his physician, Dr. W. H. Marsh of Solomons, Md., wrote: "There has been a great improvement in E. S. since his return home. He is now at work, the drowsiness has about disappeared, and there is more of a snap about his movements."

There was no opportunity to study this case thoroughly, yet the drowsiness, drooping of the lids, involuntary motions, and slow recovery were characteristic of the other cases more fully reported.

CASE 4.—*Synopsis.* Ocular, first symptoms to appear. Sudden diplopia and left internal squint. Saw a physician who used atropia. Followed by two weeks of lethargy, with very slow return of pupillary reaction. Accommodation still defective after nearly three months.

Miss X., 19 years of age, telephone operator, was sent me by Dr. C. H. Kriete of Aberdeen on March 14, 1919. She had had no recent illness. There was a left internal squint of 45°. When the left eye was excluded, the strabismus shifted to right and the excluded eye trembled. She stated that two days before, while at work as a night operator, she had suddenly seen double. A local physician, not her regular attendant, had used atropia. This was the day before

she came to me. Her refraction under atropia was: vision right, $\frac{10}{100}$, $\frac{10}{20}$ by + 2. sph., left $\frac{10}{200}$, $\frac{10}{15}$ by + 1.5 sph. The atropia had had no effect on the squint. There was definite defect in left lateral motion; the left eye would not abduct to the canthus, while the right eye would. Slight left ptosis. In view of the suddenness of the symptoms and the defective action of the left external rectus, I decided to refrain from treatment until the effects of the atropia had worn off, advising absolute rest in the meantime.

I saw her again in a week, March 21st. It was then that I first suspected lethargic encephalitis. The girl had been asleep the entire week. She would arouse and take her meals and immediately fall into a stupor. The pupils were still widely dilated and showed a barely noticeable, if any, response to light; none to convergence. She still accepted her atropia correction and the squint had disappeared. She apparently had regained about two diopters of accommodation. There was definite drooping of the left upper lid, all eye motions were good. She was lethargic during examination. She went home and slept continuously for four days. I saw her on March 25th (ten days after the use of atropia). The right pupil was the larger. Both responded to daylight and convergence. Her manifest error was a 0.5 diopter less than the total correction in the right and 0.25 in the left. She now needed +2. sph. added to her manifest error to read at 33*cm*. Correction of her manifest error was ordered for constant use.

On April 4th (just three weeks and one day after the use of atropia) the pupils were still dilated and of equal size, but reacted promptly to light. She had normal distant vision and needed one diopter added for reading at 33*cm* in the right eye (gain of one diopter of accommodation). Left eye had barely a near point of 33*cm*. (This represents for her age, according to Duane's table, a loss of accommodation of 6 to 8 diopters.) With the red glass before one eye, she developed at 20 feet a vertical homonymous diplopia correctable by 2½° prism base down before right eye.

On April 15th, she tried to resume her work. Headache and blurred vision compelled her to stop in a half-hour.

On April 21st (5½ weeks after the use of atropia) she was still about six diopters short of the accommodation normal for her age. The left pupil was larger than the right; a change since April 6th. Both reacted normally. The red glass gave homonymous, but not vertical, diplopia.

On May 12th (9 weeks and 2 days after the use of atropia) there was still inequality of the pupils but good reaction. She now had about 2½ to 3 diopters of accommodation in each eye through the glasses correcting her manifest error.

On May 25th, she had a near point of 25*cm* in the right and 20*cm* in the left eye (equal to 4 and 5 diopters of accommodation—still not over one half of the accommodation normal for her age). There was no diplopia and she was working more comfortably. She has orthophoria, distant vision. In view of the transient squint, left ptosis, lethargy, and the slow return of accommodation, I felt that the diagnosis of lethargic encephalitis was justifiable.

CASE 5.—*Synopsis.* A "cold" in January, followed by fever, lassitude, and stupor for nearly a month. At the end of that time, left, followed by right, facial paralysis, paralysis of left accommodation, periods of improvement and relapse, final recovery.

A. A., boy, 19 years old, was referred to me on April 10th by Dr. Wm. H. Pearce. So far as personal observations are concerned, there is very little for me to report. The interesting feature of the case is the early history which has been kindly furnished me by Dr. Thomas to whom Dr. Pearce sent the patient. This will be given after my own findings. He had normal central vision, no limitation of fields, a near point of 15*cm* for the right and 38*cm* for the left eye. If he looked down he developed lateral nystagmus; continuing to hold this position, the eyes became still. On looking up, there were no nystagmoid movements. They developed at once, however, on lateral motion. Pupils were of equal size and reacted normally to light and accommodation. He could shut his eyes tightly and there was no involvement of the lid.

Six days later, the boy reported that he had been very drowsy since his last visit. There were distinct tremor of the upper lids when he closed his eyes and the same nystagmoid movements on looking up, lateral motion, or convergence. The most marked change, however, was in the accommodation. The punctum proximum of the left eye had come in from 38 to 20*cm*.

The early history furnished me by Dr. Thomas shows that the boy was a student at boarding-school in Virginia, and in January, after climatic exposure, had what was supposed to be a cold. This was accompanied by dizziness and diplopia. He seems to have been more or less miserable for the next three or four weeks at school, suffering from giddiness, drowsiness, etc. Early in February (a month after the onset) he developed a left facial paralysis. He returned to Baltimore and shortly afterward the right facial nerve was involved. Dr. Thomas saw him on February 4th. He noted the expressionless face, wide open eyes, widely dilated pupils with very slight reaction to both light and accommodation; pain and nystagmoid movements on lateral motions, masse-

ters painful on pressure, almost complete double facial paralysis. At a later visit, Dr. Thomas noticed paralysis of the left accommodation, nystagmus on any lateral motion. There was gradual improvement in all of these symptoms; but all through February and March, the boy had periods of stupor and was unable to use his eyes. At times he read better than others; simply could not see the print. At the end of March he came to Dr. Pearce with complaint of pain in the region of the heart apex. Dr. Pearce found a pleuro-pericardial friction rub, which disappeared when the boy turned on right side. Pain, moderate temperature (101°) rapid pulse persisted for forty-eight hours and disappeared as mysteriously as they had come. Anorexia and prostration followed for a fortnight. I saw this boy again on May 29th. He thinks he is well and he is with the exception of lateral nystagmoid movements when he looks upward and tries to hold the eyes in this position.

I have hesitated to include the following cases.

CASE 6.—*Synopsis.* Eye symptoms first to appear. On account of age, possibility of undiscovered degenerative changes. Left abducens paralysis and dilated and feebly acting pupils only eye symptom, most of others pointed to involvement of spinal ganglia. Stupor for over two months.

Mrs. M. E., 65 years of age, was seen in consultation with Dr. J. A. Zepp on March 22d. She had been under his care for three weeks. Some weeks prior to seeing Dr. Zepp, she had been greatly frightened and since then had been nervous and sleepless. Dr. Zepp found her with double vision and vertigo. Symptoms unchanged for a week when Dr. T. B. Futcher was called in consultation. Dr. Futcher was inclined to a diagnosis of cerebral arteriosclerosis, but nothing was positive except that the diplopia was due to a weakness of the left externus.

On March 22d, the woman was in a deep stupor. This had come on three days previously. She could be aroused and a fair examination of the eyes was possible. There was partial paralysis of the left externus with jerkings and rotation at the excursion end. It was very difficult to keep her awake. Pupils were dilated and responded to light. Ophthalmoscopic appearances were negative. Other symptoms were: loss of right patella reflex and positive Kernig. Pulse 112, temperature 98°; blood pressure $\frac{165}{95}$. I felt that positive diagnosis was impossible, but it looked like lethargic encephalitis. This diagnosis was definitely made by Dr. Futcher six days later.

At that time Dr. Zepp phoned that the woman was in profound stupor and had developed right facial paralysis.

There was tenderness over the masseters. The right patella reflex had returned and the left disappeared. Kernig's sign persisted. I saw her again on March 31st. There was complete right facial paralysis, both pupils were dilated but reached slightly to light. She could move her left hand and leg very little; right normally. She had developed a tenderness on pressure along the course of the left femoral vein. Temperature 101°, pulse 110; profound stupor. A few days later she lost control of bladder and bowels. At present this still persists, more than two months after the onset of symptoms. The lethargy is beginning to lessen, but is still present. Reflexes have returned and all symptoms are clearing except the bladder and intestinal.

The diagnosis of lethargic encephalitis seems justified by the suddenness of left abducens, followed by the facial paralysis, both of which recovered; stupor and then the symptoms referable to involvement of the spinal cord.

CASE 7.—*Synopsis.* Diagnosis doubtful. Right facial neuralgia, right ptosis, total paralysis of right internus, partial of right inferior rectus; paralysis left externus. No lethargy. Death from respiratory paralysis. Possible metastasis from a previously unsuspected sarcoma of unknown situation.

Mr. A. S., merchant, 27 years old, was sent me on April 14th by Dr. Harry Goldburg. For several days Mr. S. had been suffering from severe right facial neuralgia. Dr. Goldburg wanted the eyes excluded, as cause.

Pupillary reaction, media, fundus, etc., were normal. Each eye had $\frac{20}{20}$ vision; $\frac{20}{15}$ by + 0.75 sph. correcting his manifest hypermetropia. Punctum proximum accommodation, *22cm* each, muscular balance—left hyp.—Ex. $3\frac{1}{2}$ −1° at 20 feet and only Ex. 2° at the near point. His manifest correction was ordered and Dr. Goldburg informed that I thought the eyes were at most merely a contributory cause, if that.

One week later Dr. Futcher told me over the phone that on the 18th he had seen Mr. S. in consultation. He had found a complete right ptosis and weakness of the right internal rectus. He suspected lethargic encephalitis. I saw Mr. S. that afternoon with Dr. Goldburg and found the following: he could not sleep and was very restless and anxious though rational and free from pain. There were complete right ptosis and paralysis of the right internal rectus. The right eye lagged behind the left in down motion. The pupils were small but responded to light and accommodation. Accommodation was unaffected. In left lateral motion, the left external rectus abducted the eye about half way, when the movement terminated with a few jerks and the eye rotated down and a little out. There was a

right external squint of about 20°. Dr. Goldburg was sure that the motions of the left eye were normal that morning. The man had also developed that day trouble in swallowing and vomiting. Pulse was 80, temperature, 98°. In a word, he had developed during the week since he was at my office with right facial neuralgia, paralysis of the right levator palpebræ superioris of right internal rectus, partial paralysis of the right inferior rectus without involvement of the pupils or accommodation. Between 8 A.M. and 4 P.M. of the day I saw him at his home, there had appeared partial paralysis of the left externus, vomiting, and dysphagia. That was all we found, and we all thought it a case of lethargic encephalitis. We were puzzled because of the absence of lethargy.

Three days later Dr. Goldburg phoned me that there were periodic attacks of dyspnœa. We made blood and spinal fluid Wassermann tests, and both were negative. The spinal fluid came out drop by drop without evidence of pressure. The cell count was six with slight positive globulin reaction. On Sunday, May 4th, Dr. Louis Hamburger, who was then associated with Dr. Goldburg in the case, phoned me that the man had been taken to the Union Protestant Infirmary, that he was growing rapidly worse, and, early that morning, had developed defective vision in the left eye. He also told me that a day or two before, there had been found a few palpable, small nodules in the skin of the occiput and abdomen. He had excised one from the scalp for examination. He had discovered them through the patient's complaint of pain in back of head when there was any pressure on the occiput. I saw Mr. S. about 1 P.M. He was rational, more or less in a stupor, with respiration of 40, pulse 140. Examination of the eyes was difficult and not pushed; however, I found that the muscular lesions described above persisted. When the right upper lid was raised, he saw distinctly and read, while the left was blurred. There was no apparent explanation. The man died that night of respiratory paralysis. Autopsy was not allowed.

The final point of interest in the case is the result of the study of the excised nodule. Dr. William G. MacCallum, Pathologist at the Johns Hopkins Hospital, found it a leucosarcoma. Location of the main growth is impossible; but if the symptoms were due to metastasis, they followed very accurately the course of lethargic encephalitis. The case is retained in this paper to demonstrate the uncertainty of diagnosis. The man had all the classical symptoms of lethar-

gic encephalitis except the lethargy, and numerous cases without this, but with other symptoms, have been recorded. He had been examined by two most careful diagnosticians, and if the skin nodules were present at their examinations, they were simply missed. I believe they were of later development, certainly the abdominal.

COMMENT.

Of the seven cases here reported, two gave history of antecedent influenza, one, a doubtful history, and four, no history of this disease. In view of the negative character of bacteriologic and animal experimentation, and of the undoubted frequency in which influenza has occurred previous to the onset of the lethargic encephalitis, the most reasonable view appears to be that influenza may reduce the resistance of the individual in such a way as to make subsequent infection of lethargic encephalitis more probable.

In only one of the cases herein reported was there optic neuritis, and this was of low grade. This finding is in accord with those of previous observers and also with the general lack of inflammatory and pressure symptoms which characterize the disease, and the absence of peripheral nerve involvement. In three of these (nos. 1, 4, and 5) there was serious impairment of accommodation and the pupils were dilated, sluggish, and at times inactive. In another (case 6) the age prevented accommodation tests, but the pupils presented similar conditions. These four presented other defects: in case 1, there was involvement of other branches of the 3d; in cases 4 and 6, abducens paralysis; and in Cases 1, 2, and 5, facial. While paralysis of both the extrinsic and intrinsic muscles has a tendency towards spontaneous recovery, these cases confirm the observation that the return to normal of the intrinsic is slower than that of the extrinsic muscles.

Of especial interest were the nystagmoid movements, which occurred in five of these seven cases. Indeed, in two cases they were the only signs pointing to involvement of the eye muscles. This nystagmus bore no definite relation to axis of voluntary movement of the eyes. For example, upon lateral movements of the eye as, vertical or rotatory nystagmus might appear.

How are we to explain these various muscular phenomena? The ocular symptoms are clearly of central origin. I incline to the explanation of Melland in explaining the varying clinical phenomena, according to whether the disease manifested itself as an encephalitis inferior or an encephalitis superior. In cases showing ocular muscular symptoms the disease is doubtless a polioencephalitis inferior, with lesions of the brain stem varying from the level of the anterior tubercles of the corpora quadrigemina, along the floor of the fourth ventricle to the level of the nucleus of the sixth nerve. These lesions are probably sometimes irritative, sometimes inhibitory, but never destructive. Paralysis of the intrinsic or extrinsic muscles, governed by the third nerve, is present according to the ganglion cells involved. The nystagmoid movements would thus be due to lesions involving the transverse fibers connecting the nuclei of one side with those of the other, or to lesions involving the posterior longitudinal bundle, which connects the nuclei of the third, fourth, and sixth nerves, or finally to lesions of the association fetus. The character of the nystagmus would vary according to the site of the lesion. It will be recalled that the pathology of lethargic encephalitis is merely a perivascular infiltration, the site of which may vary and the clinical symptoms will likewise vary with the site of the lesion. Paralyses of the facial, of muscles of deglutition and respiration are examples.

As to the cause of the lethargy, English observers have argued as follows, and to my mind this explanation appears very plausible. The slight fever, slight inflammatory changes in the spinal fluid, and absence of other infectious symptoms, make a toxic cause for the lethargy very improbable. The absence of optic neuritis, and other pressure symptoms, together with the generally normal tension of the cerebrospinal fluid, practically rule out increased intracerebral pressure as a cause. On the other hand, the low grade of inflammation about the brain stem might well cut off afferent impulses to the cerebrum to such a degree as to cause stupor. In conclusion, we must remember, however, that the actual cause of the disease is unknown, and the pathology still obscure. The explanations here advanced are those which, in the present state of our knowledge, appear to me most probable, but they are nevertheless, largely hypothetical.

I desire to thank Drs. G. H. Grove and G. E. W. Hardy of the Union Protestant Infirmary staff for their coöperation in observing the cases sent to the hospital.

SUMMARY.

A peculiar disease, termed "lethargic encephalitis," has been appearing sporadically throughout Europe during the last two years and has been observed in this country during the last six months. The disease is characterized by an insidious onset, lack of symptoms of an infectious nature, stupor, and involvement, sometimes paralysis, of various muscles, but chiefly the muscles of the eye or face. The ocular symptoms consist of either relative or total paralysis of the intrinsic or extrinsic muscles, ptosis, and nystagmoid movements. One or several of these symptoms may be present. The ocular symptoms have a definite tendency towards spontaneous recovery.

BIBLIOGRAPHY

1. "Epidemic or Lethargic Encephalitis" (Editorial). *Journal American Medical Association*, 1919, lxxii., 796.
2. NETTER, A. "Sur quelques cas d'encéphalite léthargique observes récemment à Paris." *Société Médicale des Hôpitaux*, March 22, 1918.
3. HARRIS, W. "Acute Infective Ophthalmoplegia of Botulism." *Lancet*, 1918, i., 568.
4. HALL, A. F. "Note on Epidemic of Toxic Ophthalmoplegia, Associated with Acute Asthenia and Other Nervous Manifestations." *Lancet*, 1918, i., 568.
5. MCCAW, H. J., PERDRAU, J. R., and STEBBING, H. F. "Toxic Bulbar Paralysis (possibly Botulism)." *Lancet*, 1918, i., 516.
6. MELLAND, C. H. "Epidemic Polioencephalitis." *British Medical Journal*, 1918, i., 559.
7. NETTER, A. "L'Encéphalite léthargique épidémique." *Bulletin de Académie de Médecine de Paris*, 1918, lxxix., 337.
8. BASSOE, PETER. *Journal American Medical Association*, 1919, lxxii., 677.
9. ELY, FRANK A. "Lethargic Encephalitis, Preliminary Report." *Journal American Medical Association*, 1919, lxxii., 985.
10. TUCKER, BEVERLEY R. "Epidemic Encephalitis Lethargica, or Epidemic Somnolence or Epidemic Cerebritis, with Report of Cases and Two Necropsies." *Journal American Medical Association*, 1919, lxxii., 1448.

11. VON WEISNER, *Weiner Klinische Wochenschrift*, July 26, 1917. (Quoted by Netter, original reference not available.)

12. "The Report of an Enquiry into an Obscure Disease, Encephalitis Lethargica. Reports to the Local Government Board on Public Health and Medical Subjects." *New Series*, No. 121, London, 1918, page 74.

OCULAR COMPLICATIONS DUE TO TYPHOID INOCULATIONS.[1]

By F. PHINIZY CALHOUN, M.D. (Atlanta, Ga.), Major, M. C., General Hospital No. 6, Fort McPherson, Ga.

IT is with reluctance that I present a subject before this Society, about which there is admittedly some doubt, but as it is not generally known that ocular lesions have been attributable to typhoid inoculations, it seems worth while at this time recording five cases of uveal infections which directly followed these inoculations, and to briefly review the literature of the subject which is exceedingly scant.

Before proceeding with the histories it is interesting to note the opinion of Lt.-Col. H. J. Nichols of the Army Medical School who replies as follows to my query: "No doubt slight effects could be found in certain cases as the eye undoubtedly will share in some of the general reactions, but I cannot believe that these effects on the eye can be of much importance, as among the vast number of men who have been inoculated and followed up in the service, we have no records of any specific damage to the eye as a result of typhoid inoculations, and so far as I know, there is no specific lesion in the eye during a course of typhoid. I have occasionally seen in rabbits corneal opacity following an intravenous injection of typhoid vaccine, but this is a non-specific effect produced by a tremendous dose."

Case 1.—Mr. B., age 35, lawyer (now a Captain of Infantry), was admitted to the First Officers' Training School at Fort McPherson, Ga., May 11, 1917, after having passed the

[1] Authority to publish granted.—S. G. O., U. S. A. Read before American Ophthalmological Society, Atlantic City, June, 1919.

usual rigid examination. On May 12th he received the first inoculation against typhoid (a triple saline vaccine). The general reaction was greater than usual and the following day the right eye became a little inflamed, and on the 14th he reported to the post hospital for treatment where he was confined and treated for an acute conjunctivitis. As the eye grew worse I (then in civil practice) was asked to see him. The picture was a typical iritis. The case was very stubborn and the pain was intense. There was no history or evidence of previous eye trouble; he denied lues, but acknowledged an old Neisser infection. A blood Wassermann was negative, but there was a slight positive reaction to a complement fixation test for gonorrhea. Teeth and gums appeared negative, as was the nose and throat examination (no X-ray). He was well, with normal vision on June 17th and was dismissed from the school. He later entered the Second Officers' Training School and graduated. I do not know that he received other inoculations, but I assume that he did.

CASE 2.—Mr. L., age 22, entered the same training school May 11, 1917, after having passed the usual physical examinations. I was told that his vision was below standard, but brought to $\frac{20}{20}$ with glasses. He received his first typhoid inoculation (triple saline vaccine) on May 14th; the second on the 20th, and the third on the 27th, with the usual general reaction. On June 1st he reported to my office complaining of blurred vision in the left eye of several days' duration. Vision was $\frac{20}{200}$, there was a slight pericorneal injection, a few dots of keratitis punctata, vitreous opacities, and an area of acute choroiditis about the size of the disk situated below the macular region, and another smaller area between the superior vessels about a disk diameter from the nerve head. There was no previous eye history, he denied lues and gonorrhea, but the blood Wassermann (civil) was positive + +. No other source of infection could be found. In due time he was rejected and returned to his home for treatment.

CASE 3.—Negro soldier, Camp Gordon, came to Eye Clinic, Emory University, sometime in July, 1917. A few days previously he had received his second typhoid inoculation (triple saline vaccine) and the left eye became inflamed the following day. Typical iritis. There was no evidence or history of previous eye trouble, and he denied venereal infections. A Wassermann was negative. He was referred to the Base Hospital of his camp for treatment.

CASE 4.—Mrs. K., age 40, seen at Emory University Eye Clinic, August 22, 1918, on account of pain in left eye. Two weeks before she took the first inoculation of typhoid vac-

cine (type unknown), the second a week later, and the third the morning of the visit with the usual reactions. The day after the second inoculation pain developed in the left eye. No history of previous eye trouble or venereal infections. The examination showed a typical iritis, with reduced vision, marked injection, and intense pain. Appropriate treatment. October 7th cured.

CASE 5.—Mrs. E., age 38, seen in consultation with Dr. A. W. Sterling, to whom I am indebted for the early history and for the privilege of reporting the case. The sight has always been defective due to a refractive error. Twelve years ago while nursing a six months' old infant, the left eye became affected and she was treated in a distant city. She did not know the diagnosis, but evidently dionin was used from the description of its reaction. After several weeks the eye was as well as ever. Her history for infection was negative, but she has always been nervous and had poor health. On July 22, 1918, she received the first inoculation against typhoid, and at weekly intervals the second and third dose with the usual reactions. The days after the last inoculation the left eye became slightly inflamed and thinking it was a cold she used household remedies, but as it grew worse and the sight became impaired she consulted her oculist. The diagnosis of uveitis with marked vitreous opacities was made at that time. Most careful physical and laboratory examinations including three Wassermanns were made to determine a cause, with negative results. When I first examined the patient six months after the onset, there was an injection of the deeper scleral vessels, the pupil was dilated, the iris slightly discolored, there were large "mutton fat" deposits on the posterior corneal surface, and a large vitreous mass, which completely obscured any fundus detail. Later the eye has cleared remarkably under thyroid tablets, but a secondary cataract has developed.

Morax appears to have been the first to have called attention to eye complications following typhoid inoculations, for in 1916 he reported his first case of a soldier, with old corneal scars dating from childhood, who developed a violent general reaction with high temperature, with herpes of the brow, eyelids, and cornea, the day after the fourth injection of antityphoid vaccine. Later he reported his second case of herpes of the face and cornea following the third injection of antityphoid vaccine in which the general reaction was intense.

Prelat the same year recorded a case of acute bilateral plas-

tic iridocyclitis following the second inoculation. The Wassermann was positive.

Rousseau later mentions a vesicular keratitis developing after an inoculation of *2cc* of triple typhoid vaccine. The general reaction was violent, and the high temperature headache and inflamed eye developed the day following the inoculation.

Bussey, of the French Medical Corps, who has had charge of the eye service in a section where twenty-two thousand troops were vaccinated against typhoid, reported that five of the men developed ocular lesions thereafter. Two had a nephritis induced by the vaccine; one, a soldier, age 45, developed albuminuric retinitis and died of uræmia; the other presented severe hemorrhage of both retinas. The three other men developed herpes and ulceration of the cornea, but they recovered without impairment of vision. Other articles of a similar nature, by Ginestous and Gloagen, appearing in foreign journals, were not accessible in the Library of the Surgeon General. It is evident that other cases must have developed in the French Army, for in 1917 the French Advisory Military Commission appointed de Lapersonne to investigate whether or not anti-typhoid inoculations could produce eye complications. His conclusions were that some eye cases had been reported which were not well established (especially those cases of acute purulent metastatic iridocyclitis due to faulty technique, poor vaccine, or latent infection in the patient), but there were a few other cases which had been closely studied, and there was strong evidence that the eye complications were directly attributable to the vaccine. He believed that the vaccine itself may produce iridocyclitis in one who previously suffered from this affection, especially when of rheumatic or syphilitic origin. He considered that there was a certain analogy between such an occurrence and the eye reactions which occasionally follow injections of tuberculin and arsenical preparations.

He further believed that there were certain hitherto unexplained lesions of the optic nerve, optic tract, and ocular palsies which may now be explained by a meningeal irritation or infection due to the reaction of typhoid vaccine. And he concluded that in order to admit the action of the typhoid vaccine inoculation, it is necessary that the ocular reaction manifest

itself at once or very soon after the injection, and where the violence of the reaction has been demonstrated by the thermometer. And he advises that the patient be subjected to an ophthalmoscopic as well as medical examination, and it would not be advisable to inoculate syphilitic, tuberculous, or arthritic patients who have had lesions of the uveal tract, especially after the fortieth year.

It is known that some cases of acute nephritis, and acute exacerbations of chronic nephritis and chronic pulmonary tuberculosis in our army as well as in the British and French armies, have been directly attributed to the typhoid inoculations. It has been suggested that the number affected is no greater than that normally found in any great body of men who have not been vaccinated. This same argument can no doubt be used against any claim the ophthalmologist might make that eye complications are directly due to these inoculations. But the fact remains that immediately following one of the inoculations certain ocular disorders developed, and circumstantial evidence is too strong to pass it up as coincidental.

One would naturally expect severe constitutional reactions associated with these eye changes; indeed, in many cases they were present, but there were others in which the reactions were normal.

No reason can be assigned for these ocular reactions other than a theoretical statement that the foreign protein contained in these vaccines has a selective action to certain eye tissues, especially the uveal layer, and that certain individuals appear to be extremely susceptible to its action. Just why the reaction in one is more severe than in another is difficult to explain. It can hardly be explained as a reaction of anaphylaxis. The bacterial suspension in the saline solution is comparatively small, yet the general reaction is greater than that of other vaccines and we are forced to accept the consideration that the endotoxin of the typhoid vaccine is the responsible element.

The *British Journal of Ophthalmology* in an editorial two years ago sounded a warning about this same question, and while we agree with the editor that "it is important that all pathological phenomena arising in patients immediately or

shortly after inoculations should be thoroughly investigated and that every endeavor should be made to determine if the relation between the vaccination and the subsequent lesions is casual or merely incidental," we believe there is now sufficient evidence to conclude that certain eye complications are directly due to antityphoid inoculations, and that:

(1) The causative factor is an endotoxin derived from the antityphoid vaccine;

(2) Observations of *sequelæ* occurring in other organs following typhoid vaccination lends support to the views herein expressed;

(3) There is an analogy between this reaction and the ocular lesions occasionally seen after the administration of tuberculin and arsenical preparations.

LITERATURE.

MORAX, V. "Nouvelle observation d'herpes palpébro-oculaire consécutif à la vaccination typhoidique." *Annal. d'oculistique.* Paris, 1916, cliii., p. 494.

—— "Herpes des muqueuses et de la cornée consecutif à la vaccination typhoidique." *Annal. d'oculistique.* Paris, 1916, cliii., p. 202.

PRÉLAT. "Un cas d'iridocyclite bilaterale au cours de la vaccination antityphoidique." *Arch. d'ophtalmologie.* Paris, 1916, xxxv., p. 742.

ROUSSEAU. "Accidents oculaires consecutif à la vaccination antityphoidique." *Arch. médicales d'Angers,* 1918, xxii., p. 34.

BUSSEY. "Disturbances in Eyes after Vaccination against Typhoid." *Lyon Medical,* 128, No. 1., p. 20, abs. *Jour. A. M. A.*

DE LAPERSONNE. "Vaccinations antityphoidique and lésions oculaires entrainant la cecité." *Arch. de Médecine et de pharmacie militaires.* Paris, 1917, lxvii., p. 236.

GINESTOUS. "Les lésions oculaires consécutif à la vaccination typhoidique." *Paris Médical,* 1917, xix., p. 150.

—— "Troubles oculaires et vaccination typhoidique." *Progrès Méd.* Paris, 1917, xxxii., p. 449.

GLOAGEN. "Herpes de la cornée consécutif à la vaccination typhoidique." *Arch. de Méd et Pharm.* Paris, 1917, ciii., p. 364.

SUBRETINAL EXUDATE SIMULATING SARCOMA OF THE CHOROID WITH ANATOMIC EXAMINATION.[1]

By DR. ARNOLD KNAPP, New York.

(With one illustration on Text-Plate XIX.)

EYES have been removed on account of a presumptive sarcoma of the choroid and have shown on microscopic examination an organized subretinal fibrous exudate. It seems of interest to put on record another case of this kind and to study the ophthalmoscopic changes with the view of determining whether these changes are definite enough to help in avoiding similar diagnostic errors.

Case History.—P. C., aged 71, presented himself at the Herman Knapp Memorial Eye Hospital on December 20, 1916, stating that the sight in the right eye had been failing for four months. The left eye was poor for some years. R. $\frac{1}{200}$, L. $\frac{1}{200}$. Patient seemed rather emaciated but otherwise healthy. Urine showed a trace of albumin and a few granular casts; the heart was negative, blood pressure 150–80; Wassermann negative. After dilating the right eye there was a sharply circumscribed detachment of the retina just in the macular region. This area seemed to be occupied by a solid subretinal mass which was dull white in color, except in the center where there was some irregular mottling. It showed an elevation of 3 D. The outlines were sharply limited. Diagnosis of sarcoma of the choroid was made and the eye was enucleated.

The *microscopic examination* of the enucleated eyeball showed in the macular region between the choroid and the retina directly springing from the choroid a triangular mass which consisted in the periphery of organized connective tissue, while in the center the tissue was of a more homogen-

[1] Presented before the American Opthalmological Society, Atlantic City, June, 1919.

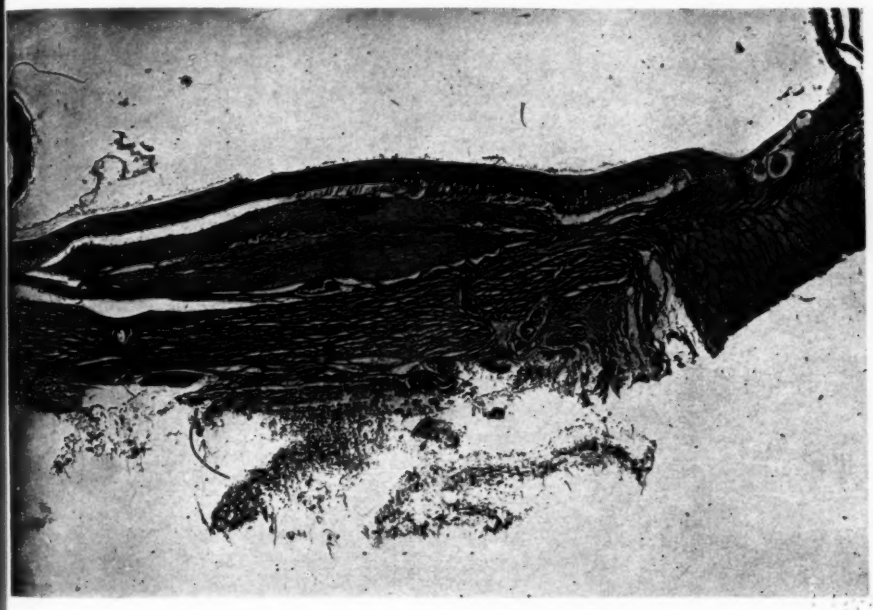
eous structure with fewer cells. Running through the center of this mass there was an irregular line of pigment, evidently the pigment epithelium with numerous gaps and a number of proliferated pigment cells extending into the surrounding tissue. The retina was adherent to this mass, the rods and cones could not be identified, the outer granular layer was scanty with the radiating supporting fibers unduly prominent, being thickened and stretched, often containing amorphous masses. The blood vessels in the retina showed no change and the central vessels in the nerve head appeared normal. The choroid itself seemed normal, except for distended vessels, whose walls were normal, without perivascular cellular infiltration. The mass was directly adherent without being continuous in structure, the character of the tissue changing immediately to flat riband-like connective tissue fibers like hyaline corneal tissue with occasional, poorly-staining, round and spindle cells and amorphous tissue without any particular characteristics. There were occasional blood vessels in the mass. To each side of the mass the separation between pigment epithelium and retina was continued by a granular amorphous exudate lined with pigmented cells.

Subsequent history: On August 28, 1918, the patient returned, complaining that the sight in the left eye had gotten worse. The sight was found reduced to counting fingers in six feet, and after dilating the pupil the eye ground presented, in addition to an inferior conus, the following changes in the macular region: On the nasal side there was a triangular deeply placed hemorrhage; adjoining this there was an area of superficial choroidal atrophy. On January 6, 1919, the condition had somewhat changed inasmuch as some dark pigment had replaced the deep hemorrhage, and there were two fresh deep-seated hemorrhages, one above and one below the original area. The patient was again seen on April 15, 1919, and showed, in addition to the pigment and deep hemorrhages in the macular region, chorioretinal changes with deep hemorrhages, connective tissue formation, and sclerosis of the choroidal vessels.

To recapitulate, the mass which was taken for a sarcoma of the choroid, on histological examination, proved to be composed of fibrous tissue presumably the result of either an organized exudate or of a blood clot. The choroid showed no inflammatory infiltration. Its vessels as well as those of the retina were normal.

A case which resembles this closely is that of R. Beatson Hird (*T. O. S. U. K.*, 1916, p. 345) who reported the case of a woman

ILLUSTRATING DR. KNAPP'S CASE OF ORGANIZED SUBRETINAL EXUDATE SIMULATING SARCOMA OF CHOROID.



aged 64, in whom the macular region was occupied by a circular pale yellowish-white area, elevated 4 D. The edges were sharply defined; a prolongation extended from one part toward the periphery and three hemorrhages were present in the surrounding retina. The retinal vessels seemed normal. The diagnosis of sarcoma of the choroid was made and the eye was enucleated. The microscope showed a tumor not connected with the choroid, consisting in a mass between the retina and pigment epithelium made up of fibrous coagulum and organized blood clot with extension of epithelial cells into the mass from the pigment epithelium and fissures from cholesterin deposits. A committee consisting of Collins, Parsons, and Mayou pronounced the case as belonging to the type of "retinitis with massive exudation" described by Coats.

Coats (*R. L. O. H. Reports*, vol. xvii., 1908, p. 440) grouped together several cases of retinal exudation sometimes associated with vascular changes occurring in young people whose general health is usually perfect. This author regards the essential pathological change to be hemorrhages in the outer layers of the retina which frequently break through externally, disintegrate, and slowly organize into cicatricial tissue. The cause for the hemorrhages is not understood; the choroid does not play an important part in the process.

Leber ("Retinitis Exudativa," *Graefe-Saemisch-Hess*, vol. vii., p. 2) believes that these changes do not follow hemorrhages but are a deep-seated inflammatory and necrosing process, often associated with hemorrhages, and that there are cases with pronounced choroidal changes. Leber does not accept Coats's view that the fibrin is derived from hemorrhage, because he has frequently observed an extensive fibrinous exudation without any blood corpuscles being present.

Friedenwald (*T. A. O. S.*, p. 819, 1914), in an article on "Retinitis with Massive Exudation," described the case of a young man, aged 18, who showed an extensive retinitis presenting a uniformly white, partly mottled surface, with peripheric hemorrhages, and two prominent masses which resembled choroidal sarcoma; the blood vessels were markedly diseased and there were vitreous opacities. The eye subsequently was enucleated and Verhoeff (*T. A. O. S.*, p. 283, 1909) on microscopic examination found large well-defined areas of

hyaline degeneration, apparently following proliferating processes with deposits of lime and cholesterin crystals.

The case which I have just reported differs from those described by Coats, principally because Coats's retinitis occurs in young persons and is generally accompanied with curious vascular changes. Of particular interest are the ophthalmoscopic changes observed in the other eye of this patient, which consisted of chorioretinitis in the macular region with deep hemorrhages and pigmentation, connective tissue formation in the retina, and sclerosis of the choroidal vessels.

Through the courtesy of Dr. H. M. Smith, of Brooklyn, I have recently observed another case of this kind in a man 69 years of age. In the macula there was a sharply defined bluish gray mass with some mottling and 4 D. of swelling. At the upper part there was a large deeply placed retinal hemorrhage. The retinal vessels showed arteriosclerotic changes and in the periphery some of the vessels were obliterated and there were new-formed connective tissue changes. The retina covering the mass showed delicate wrinkling like crackled parchment, a condition which suggests a shrinking of the underlying exudate.

It seems to me that these two cases represent a lesion in the eye ground which belongs to arteriosclerosis. This is characterized by its occurrence in the macular region in patients of advanced years. The ophthalmoscopic picture is that of a subretinal mass, sharply outlined, of moderate elevation, 3 D., bluish gray in color, with some mottling, accompanied by other arteriosclerotic changes in the same or in the other eye.

This condition is of importance in the differential diagnosis of sarcoma of the choroid. It also somewhat resembles the conglomerate tubercle; the latter condition however occurs at an earlier age, the color of the tumor is more yellowish-white, the elevation is greater, and the tuberculin test may show some local changes.

TWO CASES OF EPITHELIOMA OF THE EYEBALL AND LIDS. OPERATION. NO RETURN AFTER ELEVEN AND SIX YEARS.[1]

By DUNBAR ROY, M.D., ATLANTA.

CASE 1.—W. A. F., white, farmer, age 54. On June 10, 1908, this patient consulted me on account of a continued irritation and inflammation in his left eye.

Family history showed that father died of cancer and one brother has had cancer of the face but cured by operation.

Present history: Has always been strong and healthy. Eyes have always been good until six years ago when the left eye began to inflame. This has continued ever since with various exacerbations, always becoming worse during the warm weather.

Examination: Left eye: Considerable irritation and redness of both the bulbar and palpebral conjunctiva. Some catarrhal secretion. At the sclerocorneal margin below and to the nasal side there is an elevated gelatinous mass which resembles very much those severe cases of vernal conjunctivitis. Blood vessels were numerous, radiating from the conjunctiva into this mass. The whole sclera was congested. Pupil responded to light and accommodation. The central portion of the cornea and the upper outer quadrant were perfectly clear. There was no pain but some lacrimation. The haze in the cornea extended slightly beyond the edge of the gelatinous growth. Vision was $\frac{20}{40}$. Vision was normal in the right eye and there were no signs of irritation.

Suspecting this growth to be an epithelioma the writer removed the same as thoroughly as possible under cocaine and submitted the growth to the Pathological Laboratory of Emory University. The report received confirmed the clinical diagnosis of epithelioma. The eye healed well, but

[1] Read at meeting of the American Ophthalmological Society, Atlantic City, June, 1919.

considerable irritation persisted. The patient was then placed under Dr. Hodgson's care who used ten milligrams of radium as a local application. This treatment was continued at intervals for several months without any material results.

On February 24, 1909, eight months later, a thorough examination was again made. The patient was suffering with more pain and the whole eyeball was much congested. The gelatinous growth was still present on the cornea and had extended still farther towards the center so that there was very little clear cornea remaining. Vision was reduced to $\frac{20}{100}$. There was more infiltration in the conjunctiva, showing some extension of the growth in this direction. We then decided to enucleate the eye. This was done under ether anæsthesia and at the same time nearly all the bulbar conjunctiva was removed. The cavity was slow in healing and even the small amount of conjunctiva left began to infiltrate. A piece of this was excised and submitted for examination which also showed the epitheliomatous changes.

On March 3d, two weeks later, the whole orbital contents were exenterated leaving the upper and lower lid with every vestige of conjunctiva and cartilage removed. With the ciliæ removed from the free edge, the lids were turned back into the orbit and retained there by packing. The cavity healed perfectly and the denuded bone deep in was finally covered with epidermis.

This patient was seen one year ago and there were absolutely no signs of a return of the growth. His general health was excellent and the whole orbital cavity was smoothly covered with skin. It has now been eleven years since the operation and the result still remains excellent.

Case 2.—Mrs. Jno. W., white, age 33. November 13, 1913, this lady was referred to me by a dermatologist on account of an epitheliomatous growth extending from the lids to the eyeball.

Family history negative.

Personal history shows that the patient has always been strong and healthy up to two years ago. At that time she noticed a small ulcer at the inner canthus of the left eye at the junction of the skin and mucous membrane. This gradually increasing in size, she consulted a dermatologist. His report showed that there was a negative Wassermann and a portion of the growth excised showed a typical epithelioma. The patient was then treated constantly with varying success. Sometimes the growth would nearly heal and then break down. The treatment consisted of pastes, X-ray, and radium, changing from one to the other as the conditions demanded. For the last month it has not improved

and is beginning to involve the conjunctiva, hence this case was referred to the writer.

Examination: The patient shows absolutely no signs of cachexia which I think is perfectly characteristic of this class of malignant growths. A good portion of the lower lid shows a scabby ulceration on the dermoid side of varying extent and form. Its clinical appearance was absolutely that of an epithelioma. On the mucous membrane side there were old cicatricial scars, causing adherence to the ball. The globe itself was very red and irritated. The growth had also extended around the dermoid surface at the inner canthus and had involved the upper lid. This also showed cicatricial adhesions of the inner surface of the lid to the globe. The patient was suffering very intense pain with her eye and there was a marked superficial keratitis. After consultation it was decided that a thorough evisceration of the orbital contents together with an extensive removal of the adjacent skin offered the only hope of relief.

On Nov. 15th, two days after my first examination, the writer performed this operation under ether anæsthesia. A circular incision was made around the rim of the orbit so as to include both upper and lower lids. Internally towards the nose the skin was removed well outside of the growth. The whole orbital contents were exenterated to the apex. All oozing was checked by hot gauze compresses. The whole surface was swabbed with a strong solution of chloride of zinc followed with a packing of iodoform gauze. This dressing was not removed until the sixth day. The cavity looked healthy and the edges of the cut surfaces were beginning to granulate. She remained in the hospital two weeks following which she was brought to my office for the dressings. The same dressings of iodiform gauze were continued every three days with a complete relief of all pain and a healthy healing of the denuded surface. It was remarkable how quickly the cavity from the cut edges began to epidermatize.

Jan. 6th, nearly two months after the operation, the appearances were excellent and the skin surface was rapidly extending to the apex. May 1st, the whole cavity is covered with healthy skin. Just at the apex there was a little moisture. I then advised all dressings to be left off and for the patient to expose the cavity for one hour every day to the direct rays of the sun. In two weeks the cavity looked normal. She then passed from under my observation and a report from the dermatologist told me that two months later the inner wall of the orbit looked a little moist and irritated. This was treated with the X-ray which produced

a rapid healing. Since that time, now six years, the patient seems apparently well. I say apparently for time alone can determine whether the cure is permanent.

Remarks: Squamous epithelioma seems to be the only form of carcinoma which offers any chance of cure. Some good results have been reported from the use of the X-ray and radium. It is a well known fact that many cures of epitheliomata of the face have been reported where thorough excision with the knife has accomplished this result. Borch believes that epitheliomata of the limbus arise from the same type of epithelioma that is found in the skin and consequently these tumors should be divided into two classes: Epithelioma arising from nævi and pavement epithelial carcinoma. He thinks the former is much the most common.

On the other hand Fuchs says that if nævi at the limbus begin to grow and develop into malignant tumors it is always a sarcoma that forms from them and not an epithelioma. This author also says, to which the present writer with a limited experience agrees, that it is impossible to make a radical removal of an epibulbar epithelioma or sarcoma and for this reason enucleation or even evisceration should be done as early as possible.

Drs. de Schweinitz and Shumway, before this Society in 1913, reported the history of a case of epibulbar carcinoma, which was somewhat similar to the first case reported by the writer. Enucleation was first performed, followed later by evisceration. After eight months there had been no return.

A review of the literature on the subject has been made by these authors and the writer refers anyone to the same for a more extended review. As far as possible the writer has looked still further into the literature and has found the report of a few additional cases.

However these two, one for eleven years and the other six years, have been observed for a longer period as cured than any other similar cases which the writer has been able to find in the literature at his disposal.

There is some diversity of opinion among authors as to the proper surgical procedure after a diagnosis has been made of these carcinomatous growths. The therapeutic value of X-

ray and radium when the growth has involved the eyeball itself is certainly not very encouraging.

However the writer now has under observation a case of sarcoma in the upper lid and in the orbital cavity where he has removed the growth five times. In the last two operations 50*mg* of radium was placed in the wound for four hours, after which it was closed with silk sutures. Radium has since been used externally at various intervals and so far there has been no return of the growth. The first operation was performed six years ago.

On the other hand the early excision of the growth with an endeavor to preserve the eye has not been followed with any marked success. The immediate enucleation of the eye or even evisceration of the orbit if there is extensive involvement of the conjunctiva offers the surest result for the complete eradication of the growth.

A POSITIVE FOCAL TUBERCULIN REACTION IN A SPINDLE CELL SARCOMA WHICH HAD PERFORATED THE SCLERA.[1]

By J. W. CHARLES, M.D., St. Louis.

On July 3, 1918, B. M., 24 years old, a soda water clerk from a small town, came with the following history: Eight or nine years ago the right eye had been burned by powder. It had never given any discomfort until five years ago when the eye had been attacked by a deep pain and the patient had been compelled to stay in a darkened room. At that time he was told by an ophthalmologist that nothing could be done for his vision, which was then nil. The vision of the left eye proved to be $\frac{20}{15}$.

Inspection showed O. D. a ring staphylloma over the ciliary region in its entire upper half with a hazy spot on the cornea, at its upper limbus, the remains of a rather superficial parenchymatous keratitis; also, an almost total exclusion of the pupil in which could be seen a cataractous lens. Movement of the eyes in all directions revealed nothing until the patient looked up, when a small lump was seen on the lower inner quadrant of the sclera which seemed to originate behind the equator, was invisible in ordinary fixation, and which moved with the globe. From its curvature, its diameter was guessed at 1*cm*. Upon interrogation, the patient stoutly maintained that he had first noticed it at least one year ago and he felt sure that it was nearly eighteen months. This fact and the evidences of the old keratoscleritis compelled one to think first of all of tuberculosis because of the fact that usually progress is much more rapid after a perforation by a malignant tumor than had taken place in this case. The Wassermann reaction by Dr. Buhmann was found to be negative with the most sensitive antigen (there was no evidence or history of syphilis) and

[1] Read at meeting of the American Ophthalmological Society, Atlantic City, June, 1919.

the patient was referred to Dr. Albert E. Taussig for a diagnostic injection of tuberculin on July 5th. He found no evidences of tuberculosis in the physical examination and gave a subcutaneous injection of three milligrams of A. T. There was no evidence of a reaction until early morning of July 8th, when the patient began to have great discomfort, breakbone aching, temperature of 100.8°; the lump on the sclera was much larger, its estimated diameter being 1¾*cm*, and it was also very red, with a second lobe appearing behind and below it.

After a disappearance of several weeks, the patient returned with the report that he had been sick in bed for four days with a high temperature, but no symptoms in the respiratory tract (we had naturally thought of influenza). The patient was so loath to have an enucleation performed, although the eye was blind, that a tentative diagnosis was made of a perforating solitary tubercle and the patient was referred to Dr. Taussig for treatment with tuberculin. This was begun with 0.001*mg*, increasing the dose until August 24th, when the patient seemed to have a mild focal reaction after receiving 0.035*mg* and the growth measured in visible diameter 1½*cm* both vertically and horizontally. There was no increase in temperature and a week later the patient confessed that perhaps what made his eye red and swollen was late hours and joy-riding. Dr. Taussig went on his vacation, leaving the patient with Dr. Ross who continued to give tuberculin injections in increasing doses without any effect until the return of Dr. Taussig, October 7th, when 10*mg* were injected because no reaction had followed the administration of smaller doses up to 3*mg*.

On the following day, the growth was much redder with lacrimation and its apparent dimensions were 1¾ x 1½ x ½*cm*—in Dr. Taussig's opinion, "No doubt about a focal reaction."

The patient was immediately sent to the hospital for enucleation. After the conjunctiva had been loosened, the external rectus and the superior muscles were severed and then the optic nerve, thus shelling the globe out without injury to the tumor. This method disclosed next to the nerve a round tumor about the size of a pea connected with the middle lobe of the main growth, and which had existed unsuspected until the operation. Frozen sections from this lobe made by Dr. Ives showed an undoubted spindle-cell sarcoma (*vid.* Dr. Ives's report). No pigment could be found in the sections.

An orbital exenteration was performed by Dr. L. C. McAmis, after which a very small focus of tumor spindle-cells was found in one of the extrinsic muscles.

A course of Coley's fluid was then instituted beginning with ¼ of a minim and increasing at first ¼ daily, then in larger doses until Nov. 5th when 2 M. were given. This was followed by a slight reaction with temperature of 99.8°, pulse 88, and respiration 22; and again on the 8th when the temperature was 99.5°, pulse 90, respiration 20.

On Nov. 12th, with 2½ M. there was no reaction, nor on the 14th with 3 M., and the 16th with 3½ M.; but on the 18th, with 4 M., the temperature was 99°, pulse 74, respiration 20. Coley's fluid was continued every other day in increasing doses until Dec. 3d, when 7½ M. were given without reaction. The patient was then allowed to return home under the care of his physician. The orbital cavity has now almost completely filled out and is well covered, and eight months after the exenteration there has been no recurrence.

Dr. Ives's report follows: "The specimen consists of an eyeball and a tumor adjacent to it. The surface of the tumor is exposed excepting on the aspect adjacent to the eye. The surface is smooth. The tumor is 23 millimeters long and 15 millimeters in its broadest diameter. It is divided into three lobes by shallow fissures perpendicular to the longest diameter. The central lobe is the largest. The tumor is rather firm and the cut surface is gray-white. There is no gross evidence of areas of necrosis.

"Sections show closely packed spindle cells with elongated nuclei. The cells are arranged in bundles placed at various angles to one another. Intracellular substance is inconspicuous. A few blood vessels with thin walls were noted. Mitotic figures are fairly common.

"Diagnosis: Spindle-cell sarcoma.

"Tissue from the orbit: The tissue was examined grossly and one portion suspicious of tumor was taken for sections. This shows what I consider to be spindle-cell sarcoma."

Upon halving the globe in such a manner as to include the nerve and tumor in the same sections, the vitreous cavity was found to be about one third occupied by an almost round white growth which had detached the retina, of which there is left only a strand of tissue from the nerve to the region of the lens. The growth is situated in the lower and nasal portion and the line of the sclera can be distinctly followed in the tumor.

The fact that our ophthalmic technician is still busy in the

service has prevented a histological examination of the whole specimen, and we have been compelled to be satisfied with the undoubtedly correct diagnosis by Dr. Ives from the sections taken from the smaller posterior lobe.

A positive focal tuberculin reaction in a tumor originating in the uveal tract is explainable by considering the vascular supply of the growth. Evidently this patient had a uveal tuberculosis which gave a positive reaction, which for our purpose means a congestion in the uvea which simply extended to the tumor. Strictly speaking then the tumor itself was not positive to tuberculin but only the tissue from which it derived its blood-vessels.

The spindle-cell sarcoma is the least malignant of sarcomata and therefore we have more hope that Coley's fluid will avail in preventing recurrence. The patient was seen ten days ago with only a very small sinus remaining open.

It goes without saying that all such blind eyes in which there is any doubt whatever about malignancy should be enucleated at once for diagnosis (taking portions of any tumor for diagnosis is a dangerous practice), but the apparent extreme chronicity in the course of this tumor and apparent focal reactions to begin with, followed by the certain focal reaction October 7th, were misleading.

PERSISTENT POSTERIOR FIBROVASCULAR SHEATH OF THE LENS. A REPORT OF TWO CLINICAL CASES, AND THREE EYEBALLS EXAMINED MICROSCOPICALLY.[1]

By Dr. FRANCIS LANE, Chicago.

From the laboratory and clinics of the Illinois Charitable Eye and Ear Infirmary.

(*With 15 illustrations on Text-Plates Nos. XX.–XXII.*)

CLINICAL observations obtained from two cases of unusual cataract, and the microscopic findings of three bulbs misinterpreted for glioma, convince me that certain so-called pathologic clinical changes of the lens and anterior vitreous often indicate arrested development.

Collins, in 1892, gave a detailed anatomic description of persistent posterior fibrovascular sheath of the lens in three cases, and since then has recognized a like number of cases clinically; to him, therefore, we are greatly indebted for early valuable suggestions offering a clearer understanding of the existence of certain developmental irregularities.

Embryologists agree that the arteria hyaloidea makes its first appearance at the "greatest length" of 5*mm;* a cuticular deposit surrounds the lens vesicle in very early embryonic life, and the posterior capsule is demonstrable as such at the greatest length of 12.7*mm;* the posterior lens vesicle cells have elongated into lens fibers at a length of 13–14*mm*, and the further development of fibers continues from the equatorial region as in the adult; at the beginning of the second month the arteria hyaloidea extends through the entire optic cup as a

[1] Candidate's thesis, American Ophthalmological Society, June, 1919.

blood-carrying vessel, and ends anteriorly at the posterior pole of the lens vesicle; in the ninth week the mesodermal capsula perilenticularis goes over into the tunica vasculosa lentis, which at this stage consists only of blood vessels and surrounds the posterior half of the lens. The circulation of blood in the hyaloid ceases, the artery regresses to a solid strand and disappears simultaneously with the tunica vasculosa lentis, respectively during the sixth, seventh, and eighth months.

No satisfactory theory has been advanced to explain either the incomplete formation of the posterior capsule or the failure of the posterior cells of the lens vesicle to elongate into axial fibers. A too rapid development of the antero-posterior diameter of the secondary optic vesicle, or a failure of the elongation of the arteria hyaloidea to keep pace with the normal axial diameter of the cup, or both, might cause sufficient traction on the proverbially thin lens capsule at the region of the posterior pole to cause a laceration and permanent gap by surface expansion.

An intact capsule is impermeable to all substances except fluids. In the absence of a pigment producing intraocular foreign body, pigmentation in the lens substance must be regarded as hematogenous in origin; all the more so may this be expected if a gap in the posterior capsule exists, and the hyaloid artery persists.

Furthermore, if the hyaloidea develops to unusual caliber one might conceive how it is possible for the undifferentiated mesoderm of the capsula perilenticularis not to disappear, but to follow the laws of development and to proliferate because of over blood-supply, possibly at the expense of lens development, and by so doing favor the persistence of the arteria hyaloidea.

CLINICAL CASE 1.—Joe B., age 14. Dr. Charles Clement permits me to report this case-history, the patient having consulted him because of poor vision and an upward convergent squint of the right eye. The parents did not notice anything unusual about the eye except the squint. This was first observed when the infant was about 1 year of age.

R. V. $\frac{3}{200}$, unimproved under atropine; L. V. $\frac{20}{20}$.

The retinoscopic test in the right eye shows approximately -0.50 in the vertical, and $+1.50$ in the horizontal.

The nasal $\frac{1}{3}$ of the fairly superficial stratum of anterior

cortex is irregularly opaque at different levels with contours everywhere well defined. The opacity continues on the mesial side in a more or less fascicular manner, and likewise involves a slightly larger area of the posterior cortex. A somewhat nasally displaced, 4 x 6*mm* oval (horizontally), dense, almost chalk-like opacity without visible vascularization is seen to lie apparently on the vitreous surface of the posterior capsule. (Fig. 1.)

A 3*mm* long, narrow, vertical slit prevails above in this dense opacity, through which a red reflex is clearly visible with the ophthalmoscope, and from the same opacity five or six narrow, spindle-shaped, grayish-white striæ run forward and obliquely in downward and nasal directions. At a level between the cloudy posterior cortex and the deep chalk-white opacity are two somewhat rectangular shaped, unevenly dark-brown areas in the upper and lower nasal quadrants respectively. A reddish hyaloid artery can be traced uninterruptedly from disk to lens, if viewed from the temporal side through the wide pupil. (Figs. 1 and 2.)

Clinical diagnosis: Right upward convergent squint; congenital stationary (?) cortical cataract; blood (?) in posterior cortex; persistent posterior fibrovascular sheath of the lens, with persistent hyaloid artery.

Clinical Case 2.—Peter H., age 6, came on April 24, 1919, to my clinic at the Illinois Charitable Eye and Ear Infirmary on account of poor vision and broad excursions of both eyes. The mother furthermore volunteered the information that sometime during the summer of 1918 a neighbor called her attention to the fact that, "when the light struck his right eye a certain way the pupil 'showed up' white." Upon close questioning, she declared that at no time had the eye been red, and that the child had never complained of pain.

R. V. shadows, no red reflex; L. V. fingers at eighteen inches. Each palpebral fissure measures 21*mm;* both eyes are visibly smaller than normal, and the corneas measure alike, 8 x 9*mm*. The pupillary and ciliary zones of the iris are not definitely demarcated, and a network of delicate pupillary membrane threads stretch across the lower third of the right pupil. (Fig. 3.)

The right pupil dilates under atropine and cocaine (ad max 5*mm*), irregularly below, where three short, narrow, triangular-shaped tags of iris appear to be pulled toward the center by the pupillary threads. No pigment deposits can be found on the anterior capsule. The left pupil dilates regularly to a maximum of 5*mm*.

Completely surrounding the posterior surface of what

ILLUSTRATING DR. LANE'S ARTICLE ON "PERSISTENT POSTERIOR FIBROVASCULAR SHEATH OF THE LENS."

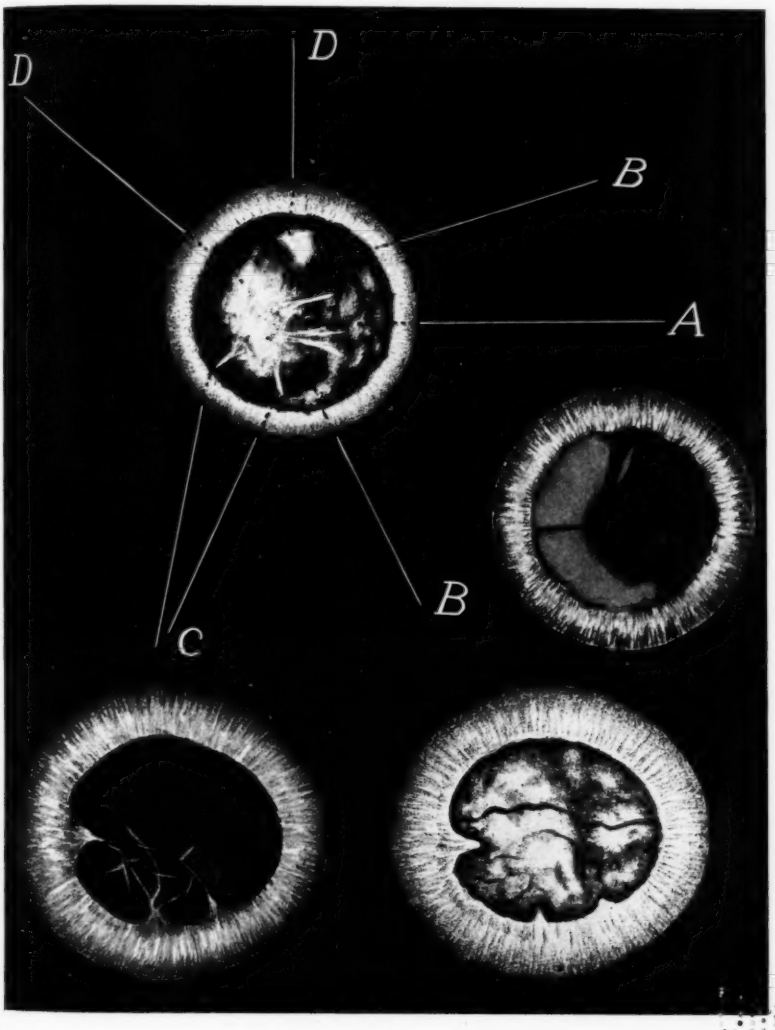


Fig. 2.

Fig. 4.

appears to be a normal lens, one sees a glistening, uniformly white opacity, on the anterior surface of which an evidently single, plainly visible, mildly tortuous vessel of fair size runs completely across in the horizontal meridian. (See Fig. 4.) Four or five much finer vessels, taking the same general horizontal course, are placed below and to the temporal side.

A less dense opacity lies immediately behind the upper nasal quadrant of the left lens, and spreads out behind the upper ¼ posterior surface as a fixed, cobweb-like network. Fundus details cannot be made out, owing to the ocular excursions. A general anæsthetic was denied for examination but I feel satisfied that a hyaloid artery is not present, and that the refractive error is in the neighborhood of +6.00.

Clinical Diagnosis: Microphthalmia, with persistent posterior fibrovascular sheath of the right lens; congenital cataract of the left lens.

The three bulbs to be described present multiple anomalies, but it is my purpose in this paper to confine the anatomic description to those anomalies only which correspond to the structures described in the two clinical cases, *i. e.*, the lens, the posterior lental opacity, and the hyaloid artery.

LABORATORY SPECIMEN A (CASE 3):

History.

When John C., apparently normal baby, became one and a half years of age, the parents first noticed a gray spot behind the left pupil. Dr. Joseph Swan observed a vascularized, white tissue behind the lens of an otherwise comparatively small eye, which, after enucleating for suspected glioma, he gave to me for microscopic examination (Nov. 12, 1907).

Gross Findings.

Left eye, 14 x 13.5 x 13.5*mm;* cornea, 7 x 8*mm*. The bulb was sectioned antero-posteriorly a trifle above the horizontal meridian. The lens, coffee-bean shaped, with the convexity forward, was apparently clear and measured 1.75 x 3.50*mm* with the long axis horizontal. It seemed to set back in a bluish-white semispherical-shaped mass, measuring 2 x 4.25*mm*, from the most posterior convex surface of which a thin thread stretched across the vitreous to the head of the optic nerve. The fine delicate ciliary processes were stretched inward and apparently attached to the most

anterior border of that part of the sheath overlapping the equatorial region of the lens.

Microscopic Findings.

The anterior capsule appears normal and the cubical cells continue around the equator, lining the posterior capsule throughout, with the exception of a few neighboring sections at the region of the posterior pole where the capsule appears to be absent, but I cannot satisfy myself that the gap is not an artefact (Fig. 6). The capsule at the equatorial region is swollen to some six microns and wavy, but gradually thins down behind to less than one micron at the posterior pole. Vacuoles, fissures, and small granular masses are scattered throughout the peripheral cortex.

Immediately behind the posterior capsule, a loosely attached, incompact, fibrous-tissue mass extends for at least $\frac{1}{2}mm$ beyond the broadest diameter of the lens both temporally and nasally. It is poor in cells and elastic fibers, but richly supplied with blood-vessels, many of which lie close to the posterior capsule (Fig. 5). The general direction of the anterior and posterior fibers of the mass is concentric with the posterior surface of the lens; particularly is this true of the posterior set, which has a laminated arrangement, while the intermediate fibers take an antero-posterior course. The hyaloid artery, filled with red blood-corpuscles, enters the membrane a trifle to the nasal side of the posterior pole of the mass, where its lumen measures $0.05mm$; it then takes a sharp bend to the temporal side, then an axial direction, and divides dichotomously. The lumen of a cross-section of the hyaloid artery, traversing the anterior vitreous, measures $0.03mm$. The ciliary processes and unretracted retina stretch inward and fuse with the anterior border of the sheath in all sections.

Anatomic diagnosis: Microphthalmia; persistent posterior fibrovascular sheath of the lens, with patent hyaloid artery attached.

Only features differing from those of Specimen A will be regarded in the descriptions of the following specimens—B and C.

LABORATORY SPECIMEN B (CASE 4):

History.

Two months after the birth of L. M., his parents noted that his right eye was smaller than his left, and, as they put it, "the pupil was discolored." When the infant was three

months old Dr. Dwight Orcutt enucleated the eye because a shallow anterior chamber and a reddish-gray reflex behind the lens suggested glioma (Jan. 27, 1908).

Gross Findings.

Right eye, 15 x 16 x 15*mm;* cornea, 8 x 9*mm.*

The pupil was round, 4*mm* across, and the entire body of the iris was pushed forward and apparently applied to the posterior surface of the clear cornea. A superior calotte was made, the vitreous was clear, and a delicate, light colored, threadlike strand began at the center of the optic nerve and ended at the center of a dense white disk on the posterior surface of the lens. With the binocular loupe the dark-lined, lengthened, ciliary processes with the unreceded retina could be seen to extend inward to the white disk behind the lens.

Microscopic Findings.

All sections show the anterior stroma of the iris passing beyond the pupillary border and becoming attached to the anterior capsule. In some specimens the entire thickness of the iris margin bends backward at right angles, but in none of the sections is there any evidence that such adhesion is caused by plastic inflammation (Fig. 7).

The cubical cells and capsule surround the entire circumference of the lens except the region of the posterior pole, where a gap in the capsule is present. A spindle-shaped, brown, finely granular structure, surrounded by pigment-bearing connective tissue cells, enters the gap, on both sides of which are a number of vacuolated cells and granular masses (Fig. 8).

Irregular, brownish areas, one quite large, dotted with small, deep-staining nuclei, are found farther forward in the cortex. (Blood ?) (Fig. 9.) The sheath behind the lens is more intimately adherent to the posterior capsule, far more cell-rich, and somewhat more vascular than that described in Specimen A. The cells consist of three types—those most posteriorly in the laminated area are markedly elongated and spindle-shaped, those in the body of the sheath are mostly oval, while anteriorly are many small round cells usually grouped about the blood-vessels. Small and abnormally large, wavy, interlacing fibers springing from the sheath and hyaloid artery (arterial diameter $\frac{1}{20}$*mm*) permeate the anterior vitreous. The ciliary processes are matted in the border of the sheath in all specimens (Figs. 10 and 11).

Anatomic diagnosis: Low grade persistent pupillary membrane; persistent posterior fibrovascular sheath of the lens, with gap of the posterior capsule; hemorrhage in the lens; persistent hyaloid artery.

LABORATORY SPECIMEN C (CASE 5):

History.

Dr. Oscar Dodd examined baby G., an infant three months old, and noted that the left lens was pushed forward on the nasal side, and a gray, vascular tissue was situated in the most anterior region of the vitreous. The tests with the ophthalmoscope and transilluminator suggested a new-growth, and the eye was enucleated for fear of glioma (Nov. 15, 1912).

Gross Findings.

Left eye, 17 x 16.5 x 16.5*mm*.

The lens measures 3 x 5.25*mm*, and the posterior sheath, displaced temporalward, is $\frac{1}{4}$*mm* thick at its greatest diameter (Fig. 12).

Microscopic Findings.

The capsule is entirely absent at the region of the posterior pole. (Fig. 13). Elongated cells and fibers from the sheath press forward into the opening for a short distance, and several near-by areas of cortex show beginning calcification. Vacuolated cells and nucleated lens-fibers stretch forward and temporalward from the connective tissue filling the gap (Fig. 14.)

The distinguishing feature of this eye lies in the fact that on the nasal side the lens-fibers are laid down normally from the equatorial region, the ciliary processes are normal, and the boundary line of the ora serrata is normally placed; whereas, on the temporal side the lining cells of the capsule continue backward to the gap, the elongated processes with the retina stretch behind the iris and fuse with the border of the posterior fibrovascular sheath (Fig. 15). So far as I am aware no like observation of the lens, ciliary body, and retina has been recorded to date.

Anatomic diagnosis: Persistent posterior fibrovascular sheath of the lens, with hyaloid artery; partial irregular development of the lens, limited to the temporal portion, constituting marked asymmetry.

As for treatment, it has been suggested that a needling, or for that matter a series of needlings, be per-

Nasal

Temporal.

Nasal.

Fig. 5. Lab. Spec. A, Case 5.

Temporal.

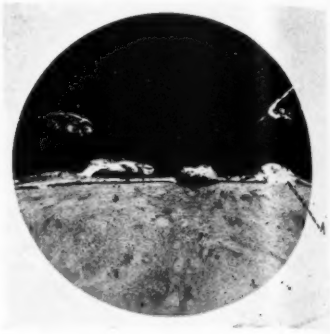
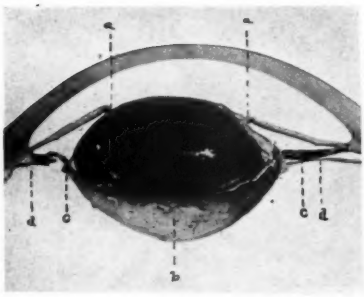


Fig. 6. Lab. Spec. A, Case 3.

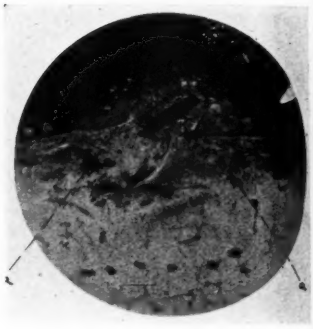
Nasal.



Temporal.

Fig. 7. Lab. Spec. B, Case 4.

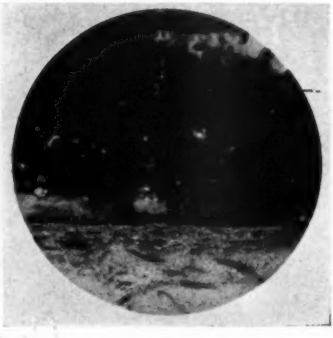
Nasal.



a

Fig. 8. Lab. Spec. B, Case 4.

Nasal.



a Temporal.

Fig. 9. Lab. Spec. B, Case 4.

Nasal.

Hyaloid Artery.

Fig. 10. Lab. Spec. B, Case 4.

ILLUSTRATING DR. LANE'S ARTICLE ON "PERSISTENT POSTERIOR FIBROVASCULAR SHEATH OF THE LENS."

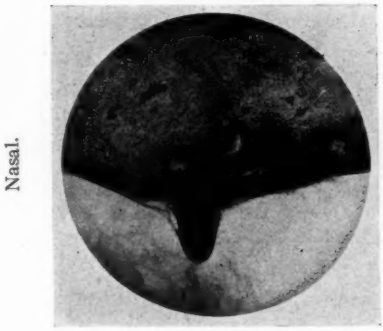


Fig: 11. Lab. Spec. B, Case 4.

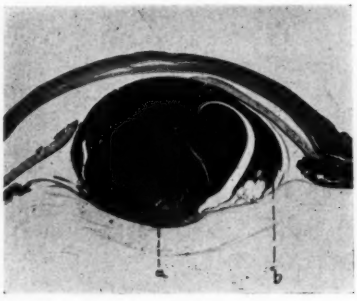
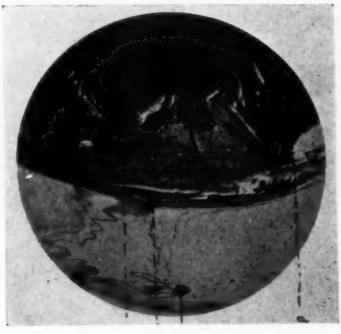


Fig. 12. Lab. Spec. C, Case 5.



a b c
Fig. 13. Lab. Spec. C, Case 5.

Fig. 14. Lab. Spec. C, Case 5.

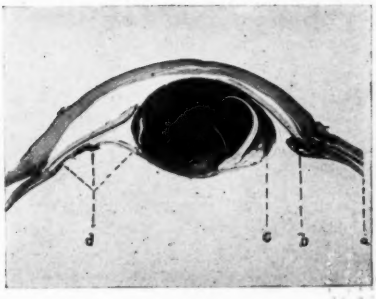


Fig. 15. . Lab. Spec. C, Case 5.

formed in the ordinary way to attain the absorption of the soft lens material. After this has been accomplished the sheath must be dealt with, because it is unaffected by contact with aqueous.

Dilacerations have been done to no avail, because the elasticity of the membrane prevents retraction of the severed surfaces. Collins advises that the mass be deliberately pushed downward and backward into the vitreous cavity. (1908.)

Should such a procedure have been successful in Cases 4 and 5, I am convinced that the anatomic relationship would have been so seriously disturbed, owing to the fusion of the sheath with ciliary processes and retina, that the eyes would have been lost from intraocular hemorrhage or glaucoma.

CONCLUSIONS.

(1) Assuming that the existing condition of the two clinical cases is congenital, it is certain that had they been examined during infancy or early childhood, the question of glioma would have been considered.

(2) An opaque, vascular tissue behind the lens, whether completely or incompletely surrounding the posterior capsule in eyes presenting evident congenital anomalies, should strongly suggest the possibility of a persistent posterior fibrovascular sheath of the lens.

(3) Pigment, particularly in the posterior portion of the lens, and a post-lental vascular membrane suggest a congenital defect of the posterior capsule and hemorrhage in the lens material.

DESCRIPTION OF FIGURES.

Fig. 1. (a) Anterior cortical cataract; (b) hemorrhage in posterior cortex; (c) striæ radiating forward; (d) persistent posterior fibrovascular sheath.

Fig. 2. Hyaloid artery.

Fig. 3. Persistent thread-like pupillary membrane.

Fig. 4. Persistent posterior fibrovascular sheath of the lens.

Fig. 5. (a) Persistent posterior fibrovascular sheath of the lens, with entrance of hyaloid artery.

Fig. 6. (a) Gap (?) of posterior capsule.

Fig. 7. (a) Persistent pupillary membrane; (b) persistent posterior fibrovascular sheath; (c) elongated processes; and (d) unretracted retina.

Fig. 8. (a) Ends of posterior capsule, with gap wedged by connective tissue.

Fig. 9. (a) Hemorrhage in lens.

Fig. 10. Vitreous fibers originating from the fibrovascular sheath, and hyaloid artery.

Fig. 11. Fibrovascular sheath, with entrance of patent hyaloid artery.

Fig. 12. (a) Persistent posterior fibrovascular sheath of the lens; (b) normal development of lens-fibers at the equator.

Fig. 13. (a) Ends of posterior capsule, with gap filled in with connective tissue; (b) entrance of patent hyaloid artery into sheath, with vitreous fibers coming from sheath, and (c) artery.

Fig. 14. Vacuolated cells, and nucleated fibers anterior to connective tissue filling gap.

Fig. 15. (a) Ora serrata; (b) normal ciliary processes; (c) normal lens-fiber development; (d) embryonic ciliary processes with unreceded retina fusing with sheath on temporal side.

ANTIDIPHTHERITIC SERUM IN SEVERE OCULAR INFECTIONS WITH SPECIAL REFERENCE TO HYPOPYON KERATITIS.[1]

By Dr. BEN WITT KEY, New York.

INTRODUCTION.

THIS branch of ocular therapeutics (serum therapy) has been characterized, more so than any other perhaps, by the most conflicting opinions and varied observations, the most enthusiastic—too enthusiastic—on the one hand, and the most conservative—too skeptical—on the other. And since Wright announced his theory of opsonins and formulated the opsonic index of phagocytic activity, investigators of every country have striven by every means of modern research to standardize bacteria and their many kindred strains, to classify their peculiarities, to measure the virulence of each, to minimize and increase this virulence, and to utilize them at will by innumerable methods of vaccination and inoculation for diagnostic, prophylactic, and therapeutic purposes. And the result of these investigations has been, that certain therapeutic means have been entrusted to the ophthalmologist, which have broadened his field of usefulness and made more directly curative the systemic ocular conditions constantly under his care and direction. For example, may I point out, briefly, the most important of these—the oldest of all methods of immunity, originated by Jenner, that of smallpox vaccination and its well-known far-reaching influence on the frequency of blind-

[1] Candidate's thesis, American Ophthalmological Society, 1919. Full report of the case histories appears in the *Transactions of the American Ophthalmological Society*, 1919.

ness; also the healing action of Behring's antitoxic diphtheritic serum upon conjunctivitis produced by Loeffler's bacilli; the effect of antitetanic serum occasionally indicated in ophthalmology; the theory and practice of serum therapy in hay-fever that is of peculiar interest to the ophthalmologist, since the use of Dunbar's "Pollantin" and Weichart's "Graminol" to the employment of those preparations, more definitely and specifically active of the present time. The Jequiritol-serum of Roemer, to combat violent Jequiritol-ophthalmia and to prevent complications, is classed as an antitoxic serum in this branch of ocular therapeutics. The field of bactericidal serum therapy, in which the pneumococcic serum of Roemer and Merk and the polyvalent serum of Roemer and others have been exploited and employed with varying results due to the practical difficulties in obtaining an autogenous or specific effect against the particular strain of organism, the same being true of streptococcal and staphylococcal serum or vaccine, the means of active immunization with vaccines from microorganisms cultivated from the eye of the patient are theoretically most acceptable, but in practice most difficult and uncertain to carry out. The gonococcic serum or vaccine effect upon metastatic iritis has proved to be most efficacious in the hands of those who have employed it, in contradistinction to its effect upon conjunctivitis where theoretically and practically the vaccine or serum has seemed ineffectual. Flexner's meningococcic serum is useful in ophthalmology through its favorable influence on the general disease; and finally, the tuberculin treatment of ocular infections as practiced by Von Hippel, Percival Hay, Maitland Ramsay, Weeks, and many others, and which has become through careful clinical observation of innumerable cases, and under the care and varied treatment of many reliable observers, a therapeutic measure of value not to be estimated.

When one recalls, then, these important therapeutic agents offered to the ophthalmologist through long continued experimental and clinical investigation, one is struck by the value of them and by the records and results, and one is stimulated to carry on, within conservative limits, the study and research of serum therapy. Following upon and coming out of the study and investigations just related, the theory and practice of para-

specific therapy has been evolved. This field, like that of the proteins, is opposed to or unexplained according to known standards of bacterial activity in the human body. Experimental and clinical results have not coincided. The older theories of immunity have not explained the results claimed by the practice of para-specific therapy. On the other hand, clinical observations of its effect have not met the demands of the fundamentals of bacteriology. The question, therefore, of the place in ophthalmology to be accorded para-specific therapy and the theory of its activity, if any, is one not as yet definitely determined.

LITERATURE.

Ophthalmic literature, since 1907, is fairly crowded with the theories, experiments, and clinical observations of many authors on this subject. Darier, perhaps more than any other, has championed the cause of para-specific therapy, and through the reports of his results, encouraged the practice of it by numerous collaborators, who more or less confirmed his findings, while at the same time he provoked a storm of criticism from those closely adherent to bacteriological principles. And so two schools of writers and investigators have arisen, who seem far apart in their theories, farther apart in their experiments, and farthest apart in their observations and analysis of results. The one holds that the use of antidiphtheritic serum in nondiphtheritic conditions of the eye is opposed by the accumulative evidence of the strictly specific reaction of the tissues against poison and foreign substance of every kind; also that it has no effect upon the opsonic index of the experimented animal, nor does it increase agglutination or complement fixation; in other words that purely experimental observations have not demonstrated that diphtheritic antitoxin is able of itself to combat nondiphtheritic ocular infections. Axenfeld (Freiburg), Happe, and von Szily made experimental tests on rabbits by previously immunizing and also treating them daily after infection with relatively large doses of Behring's and Roux's serum. Accurately measured minute quantities of culture of staphylococci or pneumococci were injected into the anterior chamber or cornea. A control rabbit was always in-

jected in the same manner. These experiments had a completely negative effect. When the injections of pneumococci were made into the vitreous the rabbits not only developed panophthalmitis, but died in a few days, exactly as did the control animals. They concluded from these experiments that the serum did not exhibit any influence against either local or general infection (*Ophthalmological Review*, page 67, 1919). It is admitted, however, that these experiments do not solve the question for the human subject. Knapp and von Michell (*Klin. Monats. f. Augenheilkunde*, 1909) warned their contemporaries against the enthusiasm over para-specific therapy, no specific results having been observed by them. Roemer (*Ophthalmology*, page 158) states that "it is self-evident from the difficulties that beset the specific etiological therapy that a nonspecific serum therapy is hopeless in ulcus serpens. Furthermore, that this fact was to have been expected from the results of the study of immunity, for there is no scientific foundation for the idea that such nonspecific serums as diphtheria serum and Deutschmann's yeast serum can possibly produce any effect upon a pneumococcal infection of the cornea." E. Janson experimented with normal rabbits and those previously treated with diphtheritic antitoxin. He used B. typhosus and para-typhosus for the agglutination experiments, and for the others he used the staphylococcus and pneumococcus. As regards agglutination, complement fixation, and opsonic index, there was no appreciable difference between the serum of the treated and the non-treated animals. Neither was there any beneficial result from treatment of experimental infections of the anterior segment of the eye. Bietta and Cavara have concluded from their work on animals, that antidiphtheritic serum is ineffective for combating post-operative experimental infections, both when injected under the skin and when administered by mouth. Neither do they believe clinical experience clearly demonstrates that antidiphtheritic serum is able of itself to combat ocular infections. The same conclusions were reached as regards experimental research with Deutschmann's serum E. and his serum D. There was no difference in the opsonic index and no change in the agglutinating power in the treated and nontreated animals.

On the other hand, Darier and his followers maintain that para-specific therapy is a means of defense of the organism in all infections, local and general; that antidiphtheritic serum is the most trustworthy of the serums employed, because of its potent eutrophic, stimulant, and anti-infective properties. They claim that its action on the organism is by its potent effect upon all the anatomic elements by placing it "in a state of defense distributed, each after its manner in the circulation,—antitoxins, immunisins, and antibodies. The glandular elements—thyroid, suprarenals, spleen, liver, testicles, and lymphatic nodes, as well as the nervous, muscular, and osseous tissues—are all in a state of organic hyperactivity." Predtetschensky insists that the antidiphtheritic serum contains "stimulins" (substances that stimulate the leucocytes to increased activity), as do other certain substances such as concentrations of nuclein acid, etc., and also horse serum (Axenfeld). Peabody, Rosenberger, Randle call attention to the effect of antidiphtheritic serum upon meningococci and state the effect is "antagonistic" and inhibits their growth similar to the action of certain microbes in nutritive media in consequence of the presence of other germs. Deutschmann has reported experiments with his yeast serum upon animals after infecting the anterior chamber with staphylococci, streptococci, pneumococci, or tubercle bacilli and the effect was markedly favorable in the rabbits infected with pneumococci. M. Neisser discovered that yeast serum in the vitreous stimulates somewhat the action of leucocytes against staphylococci, thus increasing phagocytosis. The partisans of para-specific serum therapy do not deny or doubt the specific nature of antitoxin and of the other specific antibodies, but they do adhere to the theory of para-specificity, because the process of antibacterial immunization is by no means explained by hitherto ascertained specific effects and go so far as to claim that probably the whole therapeutic effect of streptococcic and pneumococcic sera and others is an effect that may not be in itself sufficiently specific, but also acts by its nonspecific stimulating and other properties. Antidiphtheritic serum, anti-tetanic yeast serum, and normal horse serum are said to act similarly on the human subject. Of these antidiphtheritic serum has been the most popular, although whatever effect or advantage is claimed of

one is accepted as an argument to some extent in favor of all—the theory of para-specific therapy.

The accumulative evidence of clinical observation alone seems to rest on the side of para-specific serums, judging by the reports of numerous authors who have employed them. Axenfeld remarks "that clinical observation on human subjects must always speak the decisive word, although by it no mathematical certainty can be obtained and also something of subjectivity always clings to it. It is possible that a result which we do not obtain in animals may nevertheless occur in the human body." Darier heads the list of those using antidiphtheritic serum, having employed it in hundreds of cases and with results that appear unusual. His experience dates back to 1904. In *La clinique ophtalmologique*, he repeatedly defends himself and his convictions, and in this publication for 1910, p. 131, he states that his own enthusiasm during the past three years has been experienced and met with almost simultaneously in Germany and France and with absolutely different serums, and that the specific effects obtained by Roemer with his antipneumococcic serum were not as numerous or as favorable as those obtained by himself with antidiphtheritic serum or by Deutschmann, von Hippel, and Zimmermann with yeast serum and horse serum; and furthermore that the cases were now so numerous that there was no longer any doubt as to the real efficacy of para-specific therapy.

As early as 1907, Deutschmann published his experience with his yeast serum, and since that time has reported results so striking, that he has been taken to task on numerous occasions for statements difficult of acceptance. At the same time, 1907, Darier was experimenting in a similar direction with the serum of Roux and Behring, and was beginning to report most favorable results, obtained in conjunction with the usual local and surgical treatment of infections of the eye. M. Teulières, in the same year arrived at results similar to those of Darier in the use of antidiphtheritic serum. In 1908, Axenfeld threw a chill over the enthusiasm of those reporting such brilliant clinical results without experimental evidence to prove what they claimed, and appealed for a high standard of experimental and clinical work. At the same time, Happe presented the result of 100 experiments on rabbits, including infections of

the vitreous, anterior chamber, and cornea, and concluded that the value of Deutschmann's serum and antidiphtheritic serum had not been demonstrated by his experiments. Zimmermann reported eleven cases in which wounds and ulcus serpens were greatly benefited. Antonelli believed from his clinical experience that "nothing was to be feared" from the use of antidiphtheritic serum and that his results especially in severe wounds of the globe led him to advocate it. Teulières in this year concluded that the serum of Roux was undoubtedly beneficial when used in conjunction with the usual local treatment. Bailliart reported four cases of hypopyon keratitis in which he believed the result from antidiphtheritic serum was strikingly favorable. In 1909, besides Darier, who reported a large series of miscellaneous cases which he claimed to have benefited by antidiphtheritic serum, Scheuermann presented eight cases following trauma; Dehenne and Bailliart reported post-operative infections; and Dorr used it in accidental injury cases, all having noted favorable action of the serum. Deschamps reported a severe suppurative iritis following grippe and Heydar-Bey a post-grippal neuroretinitis. Angiolella reported five cases, Frogier twelve cases, Zimmermann twenty-eight cases; these observers meeting with and believing in effective results from the serum. Fernandez, J. S., ventured the use of the serum as a prophylactic measure in injuries both accidental and operative. In 1910, Deutschmann presented 117 cases treated by his "polyvalent yeast serum" and in which he claimed definitely good results; von Hippel also reported such glowing results with Deutschmann's serum that Axenfeld criticized them as being evidence of doubtful significance. Weeks in presenting the status of serum therapy in ophthalmology at Budapest was noncommittal as to the nonspecific use of diphtheritic antitoxin. During this year favorable results from nonspecific use of antidiphtheritic serum were reported by Alexandroff, Menacho, Jacqueau, Fernandez and Yvert, Piccaluga, and others. In 1911, Kasas refers to the effect of diphtheritic serum on the symptomatology of corneal ulcer and inflammation of the iris in the cases of his experience, and is impressed by the relief of pain and the definite improvement in the healing process following the use of the serum. Mayweg reported a case of panophthalmitis which was relieved by anti-

diphtheritic serum and so checked in its progress that it was unnecessary to enucleate. Darier grows bolder in urging the serum in iritis, whether tubercular, syphilitic, gonococcal, or rheumatic and suggests the use of it by mouth. During 1912, Darier, Janson, and Dorr reported further investigations, Janson giving the results of experimental work that proved the negative effect of antidiphtheritic serum and decrying the enthusiasm of the French writers, while Dorr presented 36 cases of grave corneal ulcer favorably affected by yeast serum. In 1913, Solm, R., reported experiments on rabbits with pneumococcic serum and without any result whatever, but on the other hand in man the serum showed definitely curative properties in panophthalmitis and other suppurative inflammation in which he employed it. He administered it by mouth in large doses and hypodermically. In 1914, Darier employed antidiphtheritic serum at the earliest moment in severe infections of the eye, during the period when a bacterial diagnosis is being made and during the time necessary to prepare a specific serum. This relieves pain and is usually so effectual that specific serum may be unnecessary. He urges the administration by mouth. Ribas Valero reports in detail a case of corneal abscess that resisted the usual classical treatment, and after injection of 4000 units of antidiphtheritic serum, in 72 hours there was disappearance of the purulent infiltration with marked lessening of reaction and relief of pain. During 1915, Frogier recommended oral administration of antidiphtheritic serum, and relates a wide experience in the use of the serum for paraspecific purposes. He finds it gives constant results in the relief of pain, has a definite analgesic and euphoric action, checks the infectious process, and assists in the resorption of infiltration and exudates, and in the repair of tissues. Lafont, Dupont, and Heckenroth report a series of cases treated with sera, and in forty-nine of them were most favorably impressed by the treatment. Bietti and Cavara in this year reported their experiments already referred to.

ADMINISTRATION AND DOSAGE.

Diphtheritic antitoxin has been administered hypodermically, intravenously, by the mouth and by subconjunctival

injection. It was at first employed, as was originally intended for specific purposes, by hypodermic use, and it was through this method that its apparent beneficial effect was first noted. Through a larger experience, evidently as a result of anaphylactic effects in certain cases, the oral administration has been strongly urged by its most ardent supporters, with the assurance that no general ill effects have been observed from this method and that clinical results are equally as good. Darier has advocated the subconjunctival injection in desperate cases, but his enthusiasm in this direction has not been shared by others for reason of its ultra-unscientific basis, other than by increasing local irritability and cell activity capable of any other irritating solution. Undoubtedly there have arisen anaphylactic effects sufficiently alarming to suggest the oral administration of the serum, although I have failed to find such reports in the literature. Many have observed a slight rise of temperature even to the degree of 103, with nausea, some gastrointestinal disturbances, an occasional erythema, joint pains, restlessness, etc., but which disappeared rapidly and without serious consequences. On the other hand so frequently has it been employed and without the least complication, that it is reasonable to suppose one may become careless and bold in the administration of large doses, and certain individuals sensitive to its action may suffer severely, even fatally from it. Darier claims that the antidiphtheritic serum has an action ten times more intense than normal horse serum. With 10*cc* of the serum of Roux, one obtains an effect, he says, equal to 100*cc* of horse serum. He concludes (*La Clin. Opht.*, 1913, p. 422): 1st, That with the rabbit some grave infections have been favorably influenced by serum given by mouth or by injections. In man panophthalmitis has been benefited and many other cases have been cured by the serum given by mouth. 2d, Purulent infections of the eye have been influenced more vitally and better by serum given by mouth than by injections. 3d, For prophylactic purposes the subcutaneous injection is preferable. 4th, 10 to 25*cc* a day by mouth at the first signs of infection almost invariably effects a complete cure. Mongour and Fonquet in their book *Sérum de Cheval Normal en Thérapeutique* draw the following conclusions: Horse serum is chosen by preference because it exposes less

than all others to anaphylactic accidents. 1st, It activates the coagulation of the blood, therefore is indicated in hemorrhages and more particularly in hæmophilias. 2d, It activates the hæmapoietic system and therefore is valuable in anæmias. 3d, It stimulates general phagocytosis, thereby explaining the influence upon infections and intoxications. 4th, It favors local diapedesis of white cells, thanks to its chemotactic properties, therefore is employed in burns and also in peritonitis. Furthermore they conclude that the administration by subcutaneous and by intravenous methods exposes to anaphylactic accidents, but this is not the case when given by mouth. They add that for want of normal horse serum, so difficult to obtain, one may utilize the antidiphtheritic serum which gives exactly the same results and contains the same properties.

As to the time of administration, the serum has been given at various times relative to the severity of the involvement and the employment of other treatment. It has been especially urged that it be given at the earliest possible moment after hospital treatment is demanded. The earlier the treatment is begun the more effectual is believed to be the result. Darier and his followers insist that it is often given too late just as antitetanic serum and antidiphtheritic serum for specific purposes are often administered after permanent destructive changes have taken place. On the other hand they believe that it is in the grave cases of infection where the usual local treatment, however intensely applied, may fail, that the para-specific effect administered early is of the most value. Therefore it is urged that every case be treated early, but the effect in grossly neglected cases is remarkable. As to frequency of administration, there is difference of opinion, Darier giving by mouth a moderate dose every day for three or four days. He also advocates hypodermic injections of a moderate dose every other day for three doses. Others rely upon one dose of large amount, while others have employed it every day in moderate amount by the hypodermic method. Zimmermann (Goerlitz) believes that if improvement is not definitely noted in three or four days after injection, no effect will be obtained by this therapy, but he has reported remarkable results from two injections only, and believes the effect is transient and not at all cumulative. Others share this opinion.

The usual interval between doses has been from one to three days, and I have found no instance where seven days has intervened. Together with administration of the serum, many forms of local treatment have been employed, depending for the most part on the severity and extent of the process involved in the individual case—the classic treatment of hot fomentations, atropine and local antiseptic measures, cautery (chemical and galvanic), paracentesis of cornea, transfixion of Saemisch, conjunctival autoplasty, strong dionin solution, subconjunctival injections of antidiphtheritic serum, or of salt solution, or of cyanide of mercury.

As to the dose to be administered, there are many opinions. In 1909, Darier recommended the injection of 10*cc*, equivalent to about 2500 units, and repeated every day for three days. Later, in 1913, he advocated 20*cc* by mouth, and frequently only 10*cc* in eleven times the amount of physiological salt solution by mouth was sufficient, but it may be repeated every day for three or four days if necessary. Verrey and Frogier after very large experience regard the administration of 10*cc* of serum in 110*cc* of salt solution by mouth as the best and most effectual of all the means and dosage. Piccaluga employed 800 units by hypodermic. Fernandez employed 2000 and 1000 units; Castresana (Madrid) used intravenously 10*cc* in 100 grams of solution saturated to 7%; Jacqueau (Lyon) varied the dose with the gravity of the infection, usually employing 10*cc* every day for four days. Alexandroff never gave more than 10*cc* for four injections. Zimmermann maintains that small doses are just as efficacious as, if not more so than, large doses; that 1500 units is usually sufficient and he has found it necessary to repeat it rarely. In this connection he reports 28 cases of hypopyon ulcer and infections after trauma, in which 17 cases were given only 1500 units, 3 cases given 2500 units, 5 cases given 3000 units, and 3 cases given 4000 units in all, not more than 1500 units being employed at a dose. Large doses of the serum have been administered, but those observers who have had largest experience have shown a definite preference for smaller doses repeated every day or two for three or four injections. Ribas Valero used 20*cc* hypodermically, and also Angiolella gave injections of 5000 units, both reporting very striking results. The ad-

vocates of large doses base their reasoning upon the theory of nonvascularity of the cornea, aqueous, and vitreous, which therefore require larger doses than disease elsewhere, it being claimed that these doses cause no harm and aid the ocular process by producing a negative phase of cellular activity. The minimum dose used, so far as I have been able to find, has been 500 units, while the maximum dose was 8000 units. In all the least amount regarded as necessary in a single case has been 800 units, and the maximum 15,000 units. The minimum time before a change has been observed after administration of an injection was twelve hours (this after a large dose and also after a moderate dose), the maximum time was seventy-two hours, the usual time being twenty-four to forty-eight hours. The maximum time over which the serum has been employed in a single case was six weeks, injections being given at infrequent intervals.

INDICATIONS.

The broad field of usefulness to which para-specific therapy, especially antidiphtheritic serum may be employed, should it deserve a place in ophthalmic therapeutics, is quite evident even to the casual observer. Axenfeld (Freiburg) stated at the Sheffield meeting of the British Medical Association (1908): "If one or other of the nonspecific sera should really prove so polyvalent that it is capable of acting at the same time against a number of different bacterial species, it would be a great advance." He clings here to the theory of specificity as being the necessary *sine qua non*, and does not accept the probability, founded upon innumerable clinical observations, of an action indirect or other than directly specific, to account for the effect of para-specific therapy.

Diphtheritic antitoxin has been administered for disease of almost every anatomic segment of the eye, also for the different infections to which it is exposed, as well as for prophylactic purposes. It has been employed in dacryocystitis and phlegmon of the sac, recurrent styes, persistent ulcerative blepharitis, purulent and other types of conjunctivitis, including trachoma, purulent corneal ulcer, hypopyon keratitis and abscess of the cornea, interstitial keratitis, iritis (especially

traumatic and purulent), iridocyclitis, abscess of vitreous, neuroretinitis, panophthalmitis and orbital phlegmon. Infections of the eye in which it has received most praise, include especially diphtheritic, pneumococcic and staphylococcic processes, whereas it has been tried out in all of them, particularly streptococcic, mixed infections, diplobacillary infection, influenza, syphilitic, gonorrhœal, and tubercular. For prophylactic purposes it has been used with varying degrees of speculation in cases of penetrating wounds, preoperative conditions with infection of the conjunctiva and lacrymal passages, glaucoma, traumatic cataract, etc., and following upon or incident to operative procedures of responsibility and of doubtful outcome. No statistics, however, bearing upon the efficacy of such measures have been published to my knowledge, but it has been urged on the theory of its curative value and upon the basis of its prophylactic influence from specific effects, as in the case of antitetanic serum therapy. An indication of some importance is that suggested by Darier, who emphasizes the benefits to be obtained by the early administration of antidiphtheritic serum, which is always available during the period in which a bacterial diagnosis is being made of a critically infectious condition. It is in these cases that early treatment is most needed, and to delay, while the bacterial diagnosis is being made and an autogenous or specific vaccine or serum is being prepared or procured, would lose valuable time in which perhaps irreparable damage and even loss of the globe may take place. Especially in penetrating wounds (traumatic or operative) with an infection evidently present from the clinical appearance, it is emphasized that early administration of antidiphtheritic serum may turn the tide of the process, before a specific serum or vaccine could be secured. Even then the virulence of autogenous or specific sera is so frivolous and uncertain in its preparation, dosage, and potency, that by the time it could be employed, it's specific properties may prove useless against a more advanced and more virulent process. Furthermore, in many instances specific serum or vaccine can not be had for many days, when the only treatment by that time indicated may be that of enucleation.

To record here the results from treatment with antidiphtheritic serum, as reported constantly by many authors during

the past eleven years, would make too voluminous a narrative and is quite unnecessary as a point of information or of argument. It is of real importance, however, for a thorough understanding of the subject, to summarize these results both as effecting more directly certain anatomic segments than others, and as occurring in certain infections more profoundly and definitely than in others. Suffice it to say, regarding the former that the nonvascular structures,—cornea, aqueous, lens, and vitreous—seem to have received more attention and to have been more strikingly affected than involvement of the vascular elements of the eye,—lids, conjunctiva, orbit, and uvea. Many favorable results, which however may have been due to local and other treatment, are reported in infections of the vascular parts, but these have not been such as to compete with those obtained by specific sera, which of course combats an infection of the vascular structures of the eye in the same manner as that of the skin and vascular organs of the body. It is the involvement of the refractive media, nonvascular structure, which taken together form by far the greater part of the eyeball, and in which bacteria flourish in an unusual manner, that results from para-specific therapy would seem to claim an important place in ocular therapeutics. In cases of corneal ulcer and abscess, hypopyon keratitis and infections of the anterior segment from penetrating wounds and operative procedures, actual curative processes have been insisted upon, while in panophthalmitis and abscess of the vitreous, curative reactions and amelioration of symptoms have been noted by many clinical observers. Isolated instances of phlegmon of the orbit and of the vitreous entirely cured by para-specific therapy have been cited, but so unreasonably wonderful have been these results that their real significance can not be credited. In this connection Darier has repeatedly stated that para-specific serum therapy will not cure all ocular infections any more than antidiphtheritic serum will cure all diphtheritics, nor mercury will cure all syphilitics.

As to the character of the infection involved, staphylococcic and pneumococcic infections have shown the most marked effects from the serum. Streptococcic infections have not responded at all. Its effect upon syphilitic, gonorrhœal, and tubercular infections has not been consistent in any degree,

although many reports of satisfactory results have been published. Where syphilis, gonorrhœa, or tuberculosis has been a complication of the pneumococcic or staphylococcic process in a nonvascular structure of the eye, the systemic condition has not seemed to prevent the usual effect of the serum upon the local infection.

CASES.

In my study and research of this question of para-specific therapy, I have been employing during the past two years the use of antidiphtheritic serum in many cases of severe ocular infection and have carefully observed almost daily the changes to be noted. I have also recorded a history of these cases, and a preliminary examination (appearance of the particular involvement in minute detail), as well as the course and treatment, including the dates of treatment and of definite changes in the pathological process. At this time I am able to report 30 cases—of which 23 are hypopyon keratitis, 2 infections of anterior chamber after penetrating wounds, 4 panophthalmitis, and 1 ulcus serpens.

These case histories appear in detail in the *Trans. Am. Ophth. Soc.*, for 1919.

ANALYSIS OF CASES.

In making an analysis of the cases reported above, I have striven to compile the data of all of them from the standpoint of the history, examination, serum treatment, other treatment, course, symptomatic effect and results, attempting to focus all the cases upon each point of consideration, so that a full understanding and appreciation of the effect, if any, of the serum can be studied and conclusions drawn in a clear and unbiased manner.

The first group of cases, hypopyon keratitis, twenty-three in number, are sufficiently varied in degree of severity and in extent of involvement, and are reported in sufficient detail to bear a close analysis. It is kept in mind, while studying each case, that the factors of systemic effect upon the local condition are of more real significance than those of purely local effects,

but it is obviously a difficult task to judge in many instances whether the serum has had any effect, and if so, in what degree.

Of the 23 cases of hypopyon keratitis, 18 were over forty years of age, 13 of these over fifty years. Five cases were under forty years of age and three of these were over thirty. Of the five under forty years of age, four had systemic or local conditions which *influenced* the *vitality* of the cornea; Case XI, 31 years, had an exposed cornea since childhood when his face and lids were severely burned; Case XIV, 39 years, had a 4 plus Wassermann; Case XV, 32 years, had a neglected injury of a month's standing; and Case XXII was that of a phlyctenular diathesis. The only clear cut case in which lowered corneal resistance can not be accounted for was that of Case XIII, 14 years of age, and in this case there was no increase in corneal destruction, though active over a period of 1 month, 12 days in hospital. This bears out the usual history of these cases, for it is well known that hypopyon keratitis is much more common in the aged and among debilitated individuals following upon the neglect of a local injury. In all the cases but one, a local injury was admitted, and this originated from a pustule of phlyctenular keratitis, Case XXII. The period of involvement previous to admission to hospital varied as follows: 10 in less than a week, 4 in one week's time, 4 in 2 weeks', 3 in 3 weeks', and 5 in more than 3 weeks' time.

If one studies the processes of ulceration in these cases, it is noticed that the center or near center of the cornea is involved in every case, this being the area least protected by systemic resistance, furthest from the source of nourishment (the blood). All the cases had a deep involvement of the cornea, which type usually of itself is capable of producing hypopyon. The ulcers varied greatly in size from 1½ by *2mm* to that of three quarters of the entire corneal surface. The majority of cases had an undermining of the margins of the ulcer and a periulcerative zone of infiltration characterizing the severity and progress of the infection in the individual case. This was also true of the conjunctival and iritic reaction, and in six cases definite iritic involvement complicated the hypopyon keratitis, Cases II, III, VI, XIV, XVII, and XXI. Depth of hypopyon varied from a mere line to 6*mm*, the majority being about *2mm* deep. The pneumococcus was the prevailing organism in

almost every case; in one case (VII), the staphylococcus was found to be the infecting germ; in several cases no organism was isolated or cultures failed to be made. Two cases (XIV and XVII) were complicated by syphilis.

As for treatment, similar local treatment was employed in all the cases—hot fomentations of boric acid solution where there was little danger of perforation, hot salt solution irrigations where perforation was present or imminent, bichloride vaseline (1–5000), atropine, a dressing, and bandage. The cautery employed was in every case chemical, bichloride (1–500) in less critical cases, and carbolic acid (conc.) in those most progressive and destructive in character. Bichloride was used in five cases, carbolic acid in sixteen. Instead of the Saemisch transfixion, multiple incisions through the base and margins of the ulcer were made, sometimes perforation taking place with part or complete evacuation of the aqueous and hypopyon, really amounting to a Saemisch, though in the majority of instances perforation did not take place, no attempt however being made to prevent it at this time. These incisions were made according to the method of Verhoeff in opening up an ulcerated area. With a fine La Grange knife, the blade is held with the cutting edge forward, and the tissue is divided by a forward and upward movement of the knife, each incision passing through the margin and base of the ulcer. This was performed in 16 cases, 4 of which perforated at the time of operation. Serum treatment was administered early (within 4 days) in 6 cases, within 1 week to 10 days in 6 cases, within 2 weeks or more in 11 cases. The dose varied with the severity and extent of the infection in the individual case, larger doses being given in the first six cases for one or two doses, smaller doses being used in the last 17 cases but given more frequently. The largest single dose was 5000 units, repeated in 3 days. The smallest single doze was 500 units, repeated every other day for several days (and which seemed to be effectual, Case VIII). The average dose and one most often employed was that of 2000 units followed every other day by 1000 units for four doses or less as the case demanded. The interval between doses varied from every other day to a week, in one case (XVIII) eight days intervened, and in another case (XIV) seventeen days intervened. The number of injections depended usually upon the size of the

dose and the chronicity of the involvement. One injection was sufficient in one case (XXII), twelve injections were necessary in another case (XIII), three or four injections being the average number required in the majority of the cases. The amount of serum given in a single case varied greatly, ranging from 2000 to 11000 units.

Of the most importance in this analysis is the study and comparison of the course of events in these cases following treatment as outlined above. The earliest time after injection, when the first change in the process of infection was noted, was 12 hours, when hypopyon of 1½*mm* disappeared after an injection of 1000 units, in Case XXII. The usual time intervening after an injection before a change could be noted was 24 hours, 48 hours almost invariably registering a well-marked improvement. Relief of symptoms, pain, conjunctival reaction, and iritic injection was constantly significant in 48 hours and sometimes in 24 hours following the initial serum injection. Hypopyon, promptly in 24 to 48 hours, was definitely reduced in amount or disappeared in all the cases except Cases XIV and XVII, these being syphilitic. Hypopyon disappeared slowly in four cases only; of these, two were syphilitic (cases XIV, XVII) and two with deep hypopyon (VII and XVIII). Hypopyon persisted without regard to injection of the serum only in the two syphilitic cases, but on the administration of mixed treatment rapidly disappeared. Hypopyon reappeared in seven cases, I, X, XIII, XIV, XVI, XVIII, XXIII, and disappeared promptly within 24 to 48 hours after injection of the serum in each case except Case XIV, who was syphilitic and this hypopyon yielded rapidly to mixed treatment. The iris was more or less involved in every case but more decidedly so at the initial dose of serum in Cases II, III, VI, XIV, and XVII, and responded to the injection by dilatation, freeing of synechia, and reduced reaction, except in Cases XIV and XVII, (syphilitics). As to the process of healing, I believe it is obvious that this was usually rapid, but more important still was the manner in which healing took place. There was noticed, not only in the less severe but the most severe cases, a rapid clearing away of ulcer debris such as does not usually occur in these cases, and especially of note was the transparency of the remaining not yet healed corneal tissue, the ulcer itself taking

on a clear and clean appearance early in the process of repair. In the most severe cases, with penetration and collapse of the anterior chamber, there was present in the ulcerated area a blood-suffused mass, which in 48 hours more was shedding debris from process of repair. Time required for hospital care after injection varied greatly, of course, but was commonly from ten days to three weeks, the shortest time being four days (Case XXII) and the longest, five weeks (Cases X and XIII).

Now to summarize this analysis one must necessarily view the effects and relative results of this treatment. As to the rapidity of effect, it is hardly worth while to recall the many instances related above except to point out Cases XIV and XVII where there appeared to be little or no effect and where syphilis complicated. The result of a rapidly healing and clearing away of ulcer debris left surprisingly mild opacities and in many instances vision obtained was far beyond expectations, as in Cases II, V, VII, XII, XVI, XIX, XXII, and XXIII. Those cases in which the usual treatment was administered over a long period of time and without result, and which responded promptly to injection of the serum, were Cases, III, VI, VII, VIII, IX, X, XIII, XV, and XXII. Cases in which a definite relationship appears between injection and pathological change and indicative of a pronounced systemic effect were I, II, III, IV, X, XII, XIII, XIV, XVI, XVIII, XXII, and XXIII.

Analysis of the second group of cases (B. I and II), Penetrating Wound of Cornea with infection of anterior chamber, resolves itself into the following conclusions: The course and response to treatment with preservation of the globe and useful vision obtained in each case, must be admitted to be quite contrary to the usual course of events in this type of case. I believe in case B. II that panophthalmitis was averted. Could it have been due to the serum therapy of 5000 units?

Analysis of the third group of cases (C. I, II, III, IV), Panophthalmitis, is of greater significance than it would seem at first glance. It was Aristotle who said: "That which is destroyed and can not be avoided, ceases to be of interest." The mere presence of an abscess or purulent infection of the vitreous, is sufficient in itself that the eye is beyond repair, and therefore the matter of vision and even preservation of the globe "ceases to be of interest." But so far as the observation

of the effects of antidiphtheritic serum upon the usual course and symptoms of the cases is concerned, it becomes a matter not only of interest, but one definitely expressive of the systemic effect of the serum upon an infectious process. While cure was not remotely anticipated, and not at any time was there any evidence of it, there was on the other hand evidence of curative properties in the serum, for in every case symptoms, both objective and subjective, subsided, and the infection rapidly became one of a quiet, mildly virulent type, entirely opposite to the usual course of events. Because the serum did not cure the panophthalmitis, restore the globe and some vision, can it be ruled out and be regarded as having no curative properties? Roemer says, "Anyone who regards the word serum as a miracle, is suffering under an illusion!" And yet Axenfeld concludes in his experiments on rabbits, that since the eyes went on to panophthalmitis and the animals died after injections of pneumococci into the vitreous, that the serum has no general or local effect.

The last case, D. I., Ulcer Serpens is reported in order to show that where every therapeutic means at our disposal is demanded of us and is employed, one may prevent a catastrophe.

THEORY OF EFFECT.

It seems to me unfortunate that the subject of para-specific therapy has been too excitedly and unreservedly presented to the profession, and by men, whose enthusiasm over what they observed clinically, led them to herald the serum in the very beginning of its development, as a "cure-all" of all infections regardless of a bacteriological diagnosis. Reports of "remarkable cures" by Deutschmann and his followers made it worse, for many of them were based upon opposing fundamental principles of pathology and bacteriology. So that wholly unreasonable results and reports and theories have together made the real value of para-specific therapy difficult of recognition. It must be remembered, however, that this therapy was not born of one man or two, but of a number, working along similar lines in different countries and with different products as a para-specific agent, each wholly unaware for a time (1905 to 1907) that the same theory was being studied by his

contemporary. Moreover, the whole theory of resistance and immunity during the past ten years has become more and more complicated, the more is learned about specificity, foreign proteins, activating elements of human serum, blood-cell energy, and the "kinetic" and other forces of internal secretion.

Is it a fair judgment to conclude from experiments on animals similarly infected, that in man the serum is without value? And is it a fair conclusion from purely clinical observations on cases in which intensive local treatment has also been employed, that the serum has real curative properties? This seems to me to be the crux of the situation and leaves the question in the open, with more confusion than should be, until sufficiently reliable and carefully studied history and case reports are forthcoming. And is it not true that, early in the course of an ocular infection and especially in hypopyon keratitis, the case is treated from the local standpoint too exclusively as a rule? It is astonishing how many complications (systemic) occur among these cases, for example, poor conditions of nourishment, environment, and systematic care, gastrointestinal disturbances, dyscrasias, cardio-vascular, nephritic, tubercular, syphilitic, etc. All the more, therefore, it seems to me, it behooves one to study the systemic factor in the individual case.

For these reasons and others, it has occurred to me that if one first establishes the necessity of a systemic influence in hypopyon keratitis, for the moment disregarding the virulence of the infecting organism, and then can show that there is a curative response in the infectious process to a systemic influence (serum injection), one can logically deduct that there are curative properties in the serum against the infection. With this in mind, I wish to enumerate the following observations in support of the first premise, namely that, a *systemic influence* is *present* in *hypopyon keratitis*.

1. Age is commonly past middle life.
2. Environment is usually poor and one without care.
3. Type of the undernourished.
4. Majority show some form of debilitation.
5. Primary ulcer cases.
6. Phlyctenular pustule especially.
7. Center of cornea commonly the site of deep involvement (furthest from source of nourishment).

8. Many disease complications (T. B., syphilis, nephritis, dyscrasias, etc.).

9. Many others commonly admitted.

In support of the second premise, namely that, a ***curative response*** in the ***infectious process*** follows a ***systemic effect*** from ***serum injection***, the following evidence is given.

1. Innumerable case reports from the literature show a definite response to injections of the serum as outlined above.

2. Check in progress of the infectious process in 24 hours after an injection as noted in my series of cases.

3. Relief of symptoms (pain, conjunctival and iritic reaction) in 24 to 48 hours following a dose of the serum.

4. Prompt diminution or disappearance of hypopyon in 24 to 48 hours after injection in every case reported in my series except two (these syphilitic).

5. Hypopyon returned on lapse of serum treatment and as promptly disappeared on injection of serum, as reported in 7 cases, I, X, XIII, XIV, XVI, XVIII, and XXIII.

6. Iris attachments responded to the injection in all cases except the two cases of syphilis, which responded rapidly to mixed treatment.

7. Healing process and the manner of clearing away of ulcer debris, leaving transparent corneal substance early in the process of repair, almost as distinctly noticeable a factor as the disappearance of hypopyon.

8. Rapidity of effect must be accepted.

9. Nine cases, III, VI, VII, VIII, IX, X, XIII, XV, and XXII, show response to injection immediately, although no change could be noted from previous long continued treatment.

10. Unusual effect upon cases of penetrating wounds, and especially that of purulent infection of the anterior chamber, Case B. II.

11. The resistance and defense of the tissues against the infection as demonstrated by the course and treatment of the four cases of panophthalmitis reported.

The conclusion necessarily follows that antidiphtheritic serum possesses curative properties against pneumococcic infections of the nonvascular (refractive) structures of the eye. It is of course impossible to furnish absolute proof, nor do I propose that this conclusion is absolute, in so far as the serum

being the cure is concerned or in any way the whole cure of these infections. On the other hand, local treatment is just as essential as the serum treatment, but that the systemic factor always present in every serious ocular infection must be met by serum or other treatment, as the case demands, is to my reasoning essential. In the two syphilitic cases cited above, the effect of the serum showed definite limitations, even to no effect, until mixed treatment was administered, whereas in all the other cases improvement was noted following injection of the serum, intensive local treatment being employed. Furthermore, many cases of my series, III, VI, VII, VIII, IX, X, XIII, XV, and XXII, showed definite and rapid improvement and cure, where previous to the serum injection long-continued local treatment had produced little or no effect. Case XXII especially is so indicative, particularly since this case had the accepted systemic disturbance of a phlyctenular conjunctivitis. Tuberculin had not been accepted as a valuable agent in ophthalmic therapeutics until recently, and it is not now regarded by the bacteriologist or general practitioner as of much practical value in general medicine. In fact the acceptance of its efficacy in ophthalmology now is based upon carefully studied clinical observations constantly repeated, and not at all upon experiments made on animals. Roemer's pneumococcic serum is admittedly bactericidal in effect and has curative properties, as Axenfeld admits, and yet R. Solm found no effect of the serum when experimenting on animals, while its effect in man was definitely curative. Is it to be expected then that in the face of clinical results with anti-diphtheritic serum, its apparent curative properties in man should be ruled out because of negative experimental results on animals? As for para-specificity, it came when the theory of immunity tended more and more to greater specificity, for the strains of pneumococci and menigococci, etc., act well against their particular strain of organism, one strain of the same organism being apparently ineffective or not as effective against another strain, so that the shock of nonspecificity was more abrupt than it otherwise would have been, so narrow had become the one idea of specificity of strain against strain in both passive and active immunity. Antitetanic serum, because it was not sufficiently and definitely

curative in its effect, threatened for a long time to be lost as one of the most valuable of prophylactic agencies, when its real value was being put to the test through tireless experiments and clinical observations, because it did not meet the full bacteriologic and therapeutic laws required for a cure.

The theory of how antidiphtheritic serum effects are exerted against nonspecific infections of the eye has been variously explained by the exponents of this therapy. Darier contends that strong toxins, such as antidiphtheritic or tetanus toxin, excite all the organs of the body to the production of antibodies of all kinds, not merely to the production of diphtheritic antitoxins, thus making the serum effective in all kinds of infection. It is well known that Loeffler first pointed out that the normal cornea shares in general bacterial immunity; Roemer has shown it to be true of pneumococci; and Ehrlich and Roemer proved it in regard to antitoxic immunity to the toxin of diphtheria. It is also recognized through the work of A. Leber, Roemer, Zur Nedden, and others, that receptors of the 1st order (antitoxins, agglutinins, and precipitins) pass in small quantities from the blood into the aqueous humor; on the other hand receptors of the 3d order (bactericidal substances, opsonins, hæmolysins, and cytotoxins) do not at all pass normally into the aqueous. The entrance of the latter into the aqueous has been proved after penetration, or irritation by injection or heating or chemical effects, and particularly in the presence of an inflammation. The vitreous is believed to share so slightly in any kind of immunity that, except under subconjunctival injections or violent inflammations is there any evidence at all of the presence of immune bodies. Lawford states that immunity on the part of nonvascular structures of the eye has not been confirmed; that the immunity possessed by the aqueous and vitreous is almost negligible, and even by all known means of increasing this immunity it cannot be brought up to the blood serum. He concluded that, with the exception of antidiphtheritic serum alone, therapeutic sera, both bactericidal and antitoxic, have been disappointing. He also points out that active immunization (vaccines) requires so much time that the process is not suited to an acute inflammation, although the immunity is more lasting. On the other hand, passive immunization (serums) has an effect that is im-

mediate but transient. Is it not probable that since specific sera are known to act efficaciously in the vascular structures, and not with the constancy that para-specific sera act upon nonvascular structures, there is a reason here in the anatomic structure that may be explanatory of a theory not yet understood to account for the therapeutic effect of antidiphtheritic serum upon nonspecific infections of the refractive media? What is the change, anatomic, cellular, or chemical, that takes place in the cornea and aqueous and adjacent structures, and causes the absorption of hypopyon of 1½*mm* deep in 24 hours after an injection of 2000 units of antidiphtheritic serum? The abrupt disappearance of hypopyon is one of the most unmistakable and distinctive changes that is noted in an infectious process affected by serum injection. Therefore to advance a theory that would satisfy this hypothesis should come reasonably near the solution of the effect of the serum. The composition of hypopyon is well known. In process of its formation it is believed to be an element of protection, defensive in the course of the combat, and is always significant of danger of deeper involvement or progress of the infection. That its disappearance is due to and significant of improvement in the invading process should be reasonable ground, therefore, upon which to base a curative cause for the improvement. One must keep in mind that hypopyon may disappear spontaneously without treatment, in which case it is believed to be due to the natural forces of the tissues to overcome an enemy of weaker virulence. Again it may disappear under simple local stimulative measures, when it is concluded that the natural forces by the aid of local treatment checked the invasion of an infection more virulent than the natural forces of the tissues can alone combat. Also it may disappear after local stimulation and removal of the contents of the infected area or by cauterization of it, when it is reasonable to believe that these measures directly applied gives the advantage to the natural forces of the tissues to overcome an infection whose virulence is far superior to the normal resistance of the particular individual. And so one observes that, by numerous means of increasing or stimulating the natural forces of defense, and by means of attacking the infection by direct removal or killing of the bacteria, or by weakening their virulence, hypopyon disap-

pears and repair is forthcoming. The following questions now arise: (1) Does the serum increase the natural forces of resistance? (2) Is the serum bactericidal? (3) Does it weaken the virulence of the invading organism? That the serum does produce a vital resistance is quite reasonable and is the theory usually advocated. There is certain evidence that there is a systemic element in the cause and effect of hypopyon keratitis, and the injection produces rapid improvement in the process. Whether hyperactivity of all the organs and tissues of the body and the production of antibodies with nonspecific properties is the full explanation of this effect is open to further experimentation and study. It is quite possible that the "vital energy of the tissues," so termed, may be another name for the foreign protein effect of the horse serum, regardless of the diphtheritic elements present. Piccaluga (Turin) refers to normal horse serum as possessing an hemolytic, agglutinating, and bactericidal action, as demonstrated by practical results and obtained by many experiments (Paton, Pes), and therefore concludes that in the horse there is a superproduction of elements of defense (receptors) that stimulate artificially the organism with the very virulent toxins, such as diphtheria. From the manner in which hypopyon is affected, the corneal infiltrates cleared, and ulcer debris cleaned away, it has occurred to me that there may be a determining factor of local resistance as the result of increased irrigation of the anterior segment of the eye, through a vasomotor or other effect, thereby supplying new and more highly activating leucocytes and other elements, if not increasing their number at one time, would increase their number over a given period of time. Clinical observation only lends some evidence in this direction, but further study of the physiological action of the serum, certain anatomic changes, and the local effect upon intraocular tension are necessary in order to substantiate this.

From our knowledge of bacterial processes and our study of immunization one cannot, without great reserve, believe that antidiphtheritic serum may exert a nonspecific influence against an ocular infection by the action of its contained antidiphtheritic specific elements against the bacteria of the invading process. That it has a bactericidal action is improbable, for almost invariably it is necessary to apply surgical means by

relieving an abscess or undermined margins of a deep ulcer, or cauterization, antiseptics, etc., in order to directly destroy the organism, and without which treatment the serum may not be in itself able to combat the infection.

That the serum may possess, through its diphtheritic potency and foreign protein effect, a means of reducing the virulence of nonspecific bacteria or inhibiting their growth is a factor of importance, but obviously difficult to prove. The fact that other para-specific therapy has shown similar results and these results so rapidly brought about, lends some evidence in this direction. And it seems reasonable to suppose that there is an effect directly antagonistic as well as systemic, to account for such distinctive changes as are reported. Whether this is due to a phagocytic, hemolytic, or chemotactic action, or whether by the production of nonspecific antibodies, highly poisonous or antagonistic to pneumococci, a reduction in the virulence of the infection *is* brought about and is worthy of consideration and further study. A factor in favor of this theory may be noted in the four cases of panophthalmitis reported in which a reduced virulence seems likely.

To what extent can one depend upon antidiphtheritic serum as a para-specific remedy? From our experiments clinically it would seem unreasonable to expect such a definite specific or bactericidal effect as would make it unnecessary to administer local treatment. Many cases argue decidedly against this theory. Not only are intensive local antiseptic measures essential, but also early and precise surgical means should be employed as the individual case demands. That these additions to the treatment of pneumococcic infections are demanded does not at all take away from the importance of the serum treatment, for no therapy, however efficacious, is always sufficient alone to cure. Para-specific therapy is not in any sense a "cure-all," but because it is not does not detract from its curative properties. Where the knife or the galvanic or other cautery is indicated, it should be employed regardless of any reliance upon serum therapy. But, on the other hand, where the case is seen early and serum injected, cautery or Saemisch may be prevented, due to an early checking of the disease process. Herein lies its most important therapeutic value. And, furthermore, where the process of involvement is advanced,

and the cautery or knife is indicated, early relief of pain and diminished reaction follows, as does also a rapid clearing away of ulcer debris, and final opacity of the cornea is reduced. The effect upon vision obviously is a question only of early control of the infection, rapid repair and clearing of the cornea, so that should one feel justified in relying upon antidiphtheritic serum in this regard, it can be administered before extensive destructive changes take place, and thereby be a means not only of improving but saving vision in the individual case. One does not reasonably expect the serum to alone overcome a virulent hypopyon keratitis, any more than one would look for a cure of dacryocystitis, even of a low virulent organism and treated by strong antiseptic measures with high tissue resistance, if the mechanical factor is not removed by the establishment of drainage into the nose. In the same manner proper drainage of the cornea and anterior chamber is necessary, where conditions of high virulence of the organism or an advanced process are present. The action of argyrol is known not to be bactericidal or even antiseptic as regards certain microörganisms, but its usefulness in infection is undisputed and its real effect was observed and worked out after its value was established clinically. The efficacy of antidiphtheritic serum in ocular infections is like the splint to a broken bone. The splint, though curative in its effect, may be ineffective when conditions of restlessness are present, where a bit of bone or periostium interposes as a foreign body, or specific disease, anemia, etc., may prevent healing; a cure may be finally secured through other surgical and medical therapy.

A question of special interest and importance is that of the time of administration and the dosage. I believe when more is learned of para-specific therapy, a clearer understanding of this question will give more definitely striking results. The relationship between the time of administration and the time of other treatment is of value, especially as to perforation of the anterior chamber, cauterization, hot applications, subconjunctival injections, etc. It is quite evident that the effect of an injection is transient as demonstrated by the return of hypopyon when the interval between injections was three to four days. It would be valuable to know during what time after the injection the effect of the serum is most potent, so as to time other treat-

ment. The interval between injections and the dosage to be given also presents an important relationship. My experience and that of others tends to show that 2000 units, repeated every other day, or 2000 units as an initial dose, followed daily by 1000 units for 3 or 4 doses, seems to be as efficacious as larger doses infrequently administered. And yet 1000 units alone may act remarkably upon a most resisting process, as Case XXII will certify, and similarly one dose of 5000 units affects a case in the same definite manner (I, II, III, and IV). The long period of involvement previous to the beginning of treatment must not be overlooked, for the direct effect of the serum is such that it would seem as though the tissues had already established a high local resistance and one injection checks the infection in 24 to 48 hours. In cases where the involvement is recent the infection does not advance after 48 hours, as a rule, and soon there appears evidence of repair of the tissues.

It is therefore quite probable that, with more constant and numerous effects of serum treatment and with more light upon the subject of administration and dosage in relationship to the stage of the infectious process and the time of other treatment, one may prescribe antidiphtheritic serum with more confidence in the effect than at this time it is possible to have. Its prophylactic effect, if any, can not be fairly or at all judged by previous experiments or clinical observations, for it is obvious that innumerable experiments and long research must be made for this purpose, in order to draw comparative statistical results of any value.

CONCLUSIONS.

1. Literature on para-specific therapy is an interesting study and research, and clinical reports of wide experience point toward a field worthy of being explored.

2. Favorable results with para-specific therapy are by far in the majority over unfavorable reports.

3. Antidiphtheritic serum seems to have an advantage over other para-specific agents, because it is readily obtained, its dosage is more certain and the preparation more dependable.

4. It has the advantage over specific serum and vaccines

in that it can be utilized during the time when a bacterial diagnosis is being made and the special vaccine or serum is being prepared.

5. Indications are: In all severe infections due to the pneumococcus and staphylococcus, especially hypopyon keratitis, phlyctenular pustule, penetrating wound with infection, critical ulcer of cornea, postoperative infection, and panophthalmitis.

6. It should be administered early in the course of the infection, though its effect in the late stages is even more striking than in earlier involvement.

7. Administration by hypodermic seems theoretically more practical, though its use by mouth has been strongly advocated, with results equally as good.

8. Dosage is 5000 to 2000 units, the former infrequently repeated, the latter every day for 3 or 4 doses.

9. Adverse effects seem to have been of no importance.

10. Its principal effect is probably systemic, and to some extent reduces the virulence of the invading organism through the production of antibodies.

11. Its curative properties are demonstrated by the prompt effect upon hypopyon, reduction in conjunctival and iritic reaction, clearing away of ulcer debris, and relief of pain.

12. Its effect is limited by the presence of syphilis, untreated, and also probably by other systemic conditions.

13. It cannot be depended upon solely to combat an infection, though it may be the principal means of affecting a cure. Local measures, as indicated, are essential.

14. The time of injection in relation to the stage of involvement and the time of employment of other treatment may become a matter of special consideration and value when more is learned about para-specific therapy.

15. The prophylactic use of antidiphtheritic serum at this time is only problematic.

BIBLIOGRAPHY.

ALEXANDROFF. "Sérothérapie des infections oculaires." *La Clin. Ophtal.*, 1910, p. 483.

ANGIOLELLA, D. "La Sérothérapie paraspécifique et les infections sons conjunctivales de NaCl dans les infections oculaires." *La Clin. Ophtal.*, 1909, p. 477.

ANTONELLI, V. "Discussione alla relazione di Terson al 25 Congresso della Soc. francese d'oftalm." Ref. *d'Ocul.*, 1908, p. 376.

ANTONELLI, V. "Sérothérapie paraspécifique dans les traumatismes graves du globe oculaire." *La Clin. Ophtal.*, Oct. 10, 1908, p. 305.

AXENFELD, T. *Lehrbuch der Augenheilkunde.* 1909, Jena: G. Fischer.

AXENFELD, T. "Serum-Therapy in Ophthalmology." *Ophthalmic Review*, XXVIII., 1909, p. 63.

AXENFELD, T. "Von Hippel's Estimate of Therapeutic Value of Deutschman's Serum." *Graefe's Arch. f. Ophth.*, 1910, LXXV., p. 190.

BERARD. "Un cas d'iridocyclite d'origine infectieuse guérie par le sérum de Roux." *La Clin. Ophtal.*, 1909, p. 572.

BIETTI, A., and CAVARA, V. "Sieroterapia paraspecifica nelle infezioni oculari." *Ann. di Ottal.*, 1915, vol. xliii., p. 366.

BRYAN, C. W. G. "Vaccine Therapy in Eye Diseases." *Ophthalmoscope*, 1911, vol. ix., p. 818.

CASTRESANA. "La sérothérapie dans les kératites suppurées." *Archives d' Oftal. Hisp.-Amer.*, 1912. Ref. *Clin. Ophtal.*, 1913, p. 290.

DARIER, A. "Sérothérapie des ulceres infectieux de cornée." *La Clin. Ophtal.*, Feb. 25, 1907, p. 35.

DARIER, A. "Sérothérapie paraspécifique par voie buccale, mode d' administration." *La Clin. Ophtal.*, 1909, p. 113.

DARIER, A. "Enquête sur la sérathérapie paraspécifique." *La Clin. Ophtal.*, 1910, p. 131.

DARIER, A. "Conclusions sur la sérothérapie dans les infections oculaires." *La Clin. Ophtal.*, 1910, p. 573.

DARIER, A. "Sérathérapie dans les infections oculaires." *La Clin. Ophtal.*, 1911, p. 22.

DARIER, A. "Vaccines and Serums in Ophthalmic Therapy." (Twelfth Int. Oph. Congress, Petrograd.) *Ophthalmoscope*, 1914, vol. xiii., p. 263.

DEHENNE, A., and BAILLIART. "Les resultats de la sérothérapie paraspécifique dans les cas d' infection oculaire." *La Clin. Ophtal.*, 1909, p. 357.

DESCHAMPS. "D'iritis suppurée post-grippale traite par le sérum, antidiphtérique." *La Clin. Ophtal.*, 1909, p. 364.

DEUTSCHMANN, R. "La sérothérapie paraspécifique ou polyvalente," *La Clin. Ophtal.*, 1910, p. 195.

DEUTSCHMANN, R. "Mein Heilserum." *Beitrage z. Augenh.*, 1907, Heft 69.

DORR, O. "Nouveaux resultats obtenus avec le sérum de Deutschmann." *La Clin. Ophtal.*, 1913, p. 36.

FERNANDEZ, J. S. "La kératite suppurée traitée par le sérum antidiphtérique. *La Clin. Ophtal.*, 1909, p. 365.

FERNANDEZ, F. M. "Nonspecific uses of antidiphtheritic serum." *Med. Rec.*, Nov. 6, 1910.

FROGIER. "Contribution à l'étude de la sérothérapie paraspécifique." *La Clin. Ophtal.*, 1909, p. 603.

FROGIER. "Sérothérapie paraspécifique par voie buccale dans les infections oculaires." *La Clin. Ophtal.*, 1915, vol. xxi., p. 328.

FROMAGET. "Kératites à pneumocoques guéries par le sérum antidiphtérique." *Annal. d'Oculist.*, cxxxvii., 1907, p. 59.

GALLENGA. "Traitement paraspécifique avec le sérum de Roux-Behring de certaines formes d'infections oculaires." *La Clin. Ophtal.*, 1909, p. 301.

HAPPE. "Zur nicht spezifischen Serumtherapie bei Augeninfektionen. *Bericht über die 35 Versammlung der Ophthal. Gesell. Heidelberg*, 1906, p. 141.

HAPPE. "Experimentelle Untersuchungen zur nicht spezifischen Serumtherapie." *Klin. Monatsbl. f. Augenheilk.*, XLVII. Beilageheft, Jahrg. 1909." (Neue Folge, VII. Band), p. 140.

HEYDAR-BEY. "Neuro-retinite post-grippale (guérison par le sérum antidiphtérique). *La Clin. Ophtal.*, 1909, p. 307.

VON HIPPEL, A. "Discussione alla comunicazione di Happe. Zur nicht spezifischen bei Augeninfektionen." *Bericht über die 35 Versammlung der Ophthal. Gesell. Heidelberg*, 1908, p. 155.

VON HIPPEL, A. "Ueber Serumtherapie bei Augenerkrankungen. Versammlung Niedersachsischer Augenarzte in Göttingen 31, V. 1908. Ref. *Klin. Monatsbl. f. Augenheilk.*, XLVI. Jahrg., VI. Band, p. 87.

JANSON, E. "Influence of Antidiphtheritic Serum on Infectious Diseases of Eyes." *Klin. Monats. f. Augenh.*, May, 1912, p. 654. *Ophthalmoscope*, vol. ii., p. 692.

JAQUEAU. "Enquête sur la sérothérapie paraspécifique." *La Clin. Ophtal.*, 1910, p. 284.

KASAS, J. "Antidiphtherieserum bei Augenkrankheiten." *Zeit. f. Augenh.*, 1911, xxv., p. 579.

LAFONT, A., and DUPONT, V. "Sérothérapie." *La Clin. Ophtal.*, 1915, vol. xxi., p. 364.

LAWFORD, J. B. "Intraocular Therapy in Eye Diseases." *Tr. Ophth. Soc. United Kingdom*, 1911, xxxii., p. 1.

MAYWEG, S. "Ueber Wirkung des Diphtherieserums bei eitrigen Prozessen des Auges." *Klin. M. f. Augenh.*, April, 1912, p. 470.

MENACHO, M. "Suppuration tardive dans l'opération de la cataracte avec insucces de la sérothérapie paraspécifique." *Arch. d'Oftal. Hisp.-Amer.*, x., p. 15. Ref. *La Clin. Ophtal.*, 1910, p. 134.

MONGOUR et FONQUET. "Sérum de cheval normal, son utilisation en thérapeutique." Pub. in Paris, 1912.

NEISSER U. GUERRINI. "Ueber Opsonine und Leukostimulantien." *Arbeiten aus dem Königl. Institut. f. experim. Therap. zur Frankfurt a. M.*, 1908. Heft 4.

PICCALUGA. "La sérothérapie paraspécifique par voie sous-conjunctivale et hypodermique." *La Clin. Ophtal.*, 1910, p. 228.

RIBAS VALERO. "Seroterapia Paraspecifica." *Archiv. de Oftalmologia*, 1914, vol. xv., p. 13.

ROEMER. "Discussione alla comunicazione di Happe zur nicht spezifischen Serumtherapie bei Augeninfektionen." *Bericht über die 35 Versammlung der Ophthal. Gesell. Heidelberg*, 1908, p. 153.

ROEMER. *Textbook of Ophthalmology*, 1913.

ROEMER. "Experimentelle und Klinische Grundlagen für die Serumtherapie der Pneumokokkeninfektion der menschlichen cornea (Ulcus serpens)." Wiesbaden, 1909.

SCHEUERMANN, W. "Contribution à la sérothérapie paraspécifique ou polyvalente avec le sérum antidiphtérique." *La Clin. Ophtal.*, 1909, p. 72.

SOLM, R. "Die interne Serumtherapie bei eitrigen Augenentzundungen." *Therapeut. Monats.*, vol. xxviii., 1914, p. 111.

TEULIÈRES, M. " Die Serotherapie bei Schweren Infektion des Auges." *Die Ophth. Kl.*, April 10, 1908.

TEULIÈRES, M. "La sérum antidiphtérique dans le traitement de la kératite à hypopyon." *La Clin. Ophtal.*, 1909, p. 240.

VERRY, L. "Un cas d'iritis aigue traite par le sérum antidiphtérique par voie buccale." *La Clin. Ophtal.*, 1909, p. 302.

WEEKS, J. E. "Serum and Vaccine Therapy in Ophthalmology." *Tr. Sixteenth International Cong. Med., Budapest*, 1909.

WEEKS, J. E. "Status of Vaccine and Serum Therapy in Ophthalmology." *Trans. Sec. on Ophth. A. M. A.*, 1910, p. 356.

YVERT, A. "Les applications paraspécifiques ou polyvalentes du serum antidiphtérique." *Recueil d'Opht.*, 1910, xxxii., p. 129.

ZIMMERMANN. "Contribution à la sérothérapie de Deutschmann." *La Clin. Ophtal.*, Sept., 1908.

ZIMMERMANN. "Nouvelle contribution à la sérothérapie paraspécifique des affections oculaires." *Clin. Ophtal.*, 1909, p. 9.

ZUR NEDDEN, M. "Experimentelle Untersuchungen über das Vorkommen baktericider Substanzen im Auge nicht immunisierter Individuen. *Graefe Archiv. f. Ophth.*, 1907, lxv., 2.

REPORT ON THE TEACHING AND EXAMINATION OF MEDICAL STUDENTS IN OPHTHALMOLOGY.

COUNCIL OF BRITISH OPHTHALMOLOGISTS.

1. *Permanent Members:*

Being the Presidents (past and present) of the Ophthalmological Society of the United Kingdom, and of the Section of Ophthalmology of the Royal Society of Medicine.

Sir ANDERSON CRITCHETT, Bt., C. V. O. (President)
Sir JOHN TWEEDY (Vice-President)
Mr. PRIESTLEY SMITH (Vice-President)
Sir GEORGE BERRY
Mr. F. RICHARDSON CROSS
Mr. J. B. LAWFORD (Treasurer)
Mr. W. LANG
Mr. E. TREACHER COLLINS
Mr. J. B. STORY
Mr. W. T. HOLMES SPICER

2. *Elected Members:*

a. By the Ophthalmological Society of the United Kingdom:

Mr. J. GRAY CLEGG
Colonel J. HERBERT PARSONS
Mr. STEPHEN MAYOU
Mr. A. B. CRIDLAND

b. By the Section of Ophthalmology of the Royal Society of Medicine:

Mr. J. HERBERT FISHER
Dr. GEORGE MACKAY

Mr. W. G. LAWS
Mr. LESLIE PATON (Hon. Secretary)

c. By the Oxford Ophthalmological Congress:
Mr. P. H. ADAMS

The Council appointed the following:

Mr. J. B. Lawford (Chairman), Sir John Tweedy, Messrs. Collins, Mackay, Clegg, Adams, Mayou, and Paton to be a committee to consider the question of the teaching and examination of medical students in ophthalmology and to report to the Council on the steps that should be taken to improve this training.

The Council have considered the question of the teaching and examination in ophthalmology before qualification, and report as follows:

PART I.—Representations to the General Medical Council on the subject.

PART II.—Existing regulations concerning the teaching and examination in ophthalmology in the United Kingdom and abroad.

PART III.—The need for improved instruction of medical students in ophthalmology.

PART IV.—Summary of recommendations.

Part I.—Representations to the General Medical Council on the Subject.

By the courtesy of the General Medical Council the following information has been obtained.

In 1879, twenty-four prominent ophthalmic surgeons presented a petition to the General Medical Council advising a compulsory three months' course in practical ophthalmology for medical students, and pointing out to the Council the neglect of training in this subject as compared with Continental and Indian Universities. As the result of this petition the General Medical Council approached the various examining bodies in the United Kingdom, and subsequently made the following recommendation:

"With reference to ophthalmology, the opinion of the bodies is almost unanimous that, under the present arrangements of their respective examinations, the subject of ophthalmology receives its fair share of attention, and that it would not be desirable, either to require attendance on a special course of lectures on ophthalmology as part of the curriculum for a medical student, or to make ophthalmic surgery a distinct subject of examination (separate from surgery) at the Pass Examination for a License to practice. The Committee[1] see no reason to dissent from that opinion of the licensing bodies, and they accordingly do not advise the Council to recommend that a special course of study of ophthalmology, or a distinct examination in that subject, should be required."

On May 29, 1891, the Ophthalmological Society of the United Kingdom[2] presented a memorial to the General Medical Council in favor of including ophthalmic medicine and surgery in the ordinary curriculum. This was received by the Council, and entered on their minutes, but no further action was taken at the time.

On May 26, 1906, the General Medical Council approved a report of their Examination Committee that: "The Inspectors called attention to the circumstance that at some Boards no evidence of knowledge of ophthalmology was required."

On November 26, 1910, the General Medical Council adopted a report of their Education Committee as follows:

"In the curriculum of all the licensing bodies, with three exceptions, special courses on ophthalmology form an essential part. The Committee are of opinion that every student of medicine should receive some special instruction in the subject. The Committee do not think it necessary to insist that every student should be examined in ophthalmology, but they are of opinion that all students should be liable to be examined in some branch of the subject."

In 1911, a communication from the British Medical Association, asking that the study of ophthalmology should be made compulsory in the medical curriculum, was brought before the General Medical Council. In reply the attention of the British

[1] *I.e.*, The Education Committee of the General Medical Council.

[2] *Trans. Oph. Soc. U. K.*, vol. xii., 1892, p. 225.

Medical Association was called to the report by the Education Committee in November, 1910, cited above.

Part II.—Existing Regulations Concerning the Teaching and Examination in Ophthalmology in the United Kingdom and Abroad.

The present condition of Ophthalmic Training and Examination in Great Britain and Abroad.

A circular letter was sent to the principal universities and other examining bodies at home and among the allied and neutral countries. In consequence of the war, the circular probably failed to reach some of those to whom it was addressed.

Answers have been received from twenty-two examining bodies in Great Britain and Ireland and from twenty-six colonial and foreign universities.

A. The Teaching and Examination in Ophthalmology in the United Kingdom.

(1) The requirements as to training are as follows:

a. No certificate of training in ophthalmology required.

University of Oxford.
University of Cambridge.

b. Ophthalmology one of four optional special subjects, certificates required for two only.

The Society of Apothecaries of London.

c. A certificate of attendance at an ophthalmic clinic for three months required.

University of London.
" " Liverpool.
" " Aberdeen.
" " Dublin. Trinity College.
Queen's University of Belfast.
Conjoint Board R.C.S. England and R.C.P. London.
" " R.C.P. and S. Edinburgh and R.F.P. and S. Glasgow (13 attendances).
" " R.C.P. and S. Ireland.

d. Certificates of attendance on a course of lectures and clinical instruction required.

University of Edinburgh.
" " Glasgow.
" " St. Andrews.
" " Wales.
" " Durham.
" " Birmingham.
" " Manchester.
" " Sheffield.
" " Bristol.
" " Leeds.
National University of Ireland.

(*e*) The methods of examination are as follows:

a. An occasional question in the surgery paper, or *viva voce;* the examiners not being ophthalmic surgeons.

University of Oxford.
" " Cambridge.
" " London.
" " Durham.
" " Leeds.
" " Sheffield.
" " Bristol.
" " Glasgow.
" " Aberdeen.
" " Wales.
Conjoint Exam. Board R.C.S. England and R.C.P. London.
" " " R.C.P. and S. Edinburgh and R.F.P.S. Glasgow.
Society of Apothecaries of London.

b. Special examination conducted by ophthalmic surgeons as part of the qualifying examination.

University of Dublin, Trinity College.
National University of Ireland.
Queen's University of Belfast.
Royal Coll. of Phys. and Surg. Ireland.

University of Liverpool.
" " Birmingham.
" " Manchester.

c. Class examinations. The certificates required before admission to the qualifying examination given only to students who attend a recognized course regularly and reach a defined standard in the class examinations.
University of Edinburgh.
" " St. Andrews. (Commencing 1919).

(The regulations under (*a*) also apply to these two universities.)

B. The Teaching and Examination in Ophthalmology in Colonial and Foreign Universities.

America. The report of the Carnegie Trust on Medical Education in America has been of great assistance to the Council in selecting the universities to which circulars should be sent.

United States.

University of Michigan, Ann Arbor.
Johns Hopkins University, Baltimore.
Harvard University, Boston.
Northwestern University, Chicago.
University of Illinois, Chicago.
Rush Medical College, University of Chicago.
Western Reserve University, Cleveland.
University of Kentucky, Louisville.
" and Bellevue Medical College, New York.
" " Columbia, New York.
" " Cornell, New York.
Yale University.

Canada.

McGill University, Montreal.
University of Toronto.

All the above, with the exception of the Northwestern University, Chicago, require students to attend both a course of lectures and a course of clinical instruction, and hold special examinations conducted by ophthalmic surgeons. The North-

western University, Chicago, require a certificate of attendance on a course of clinical instruction in ophthalmology and there is no special examination.

France.

University of Paris.

Clinical course in fourth year. Certificate after examination.

University of Toulouse.

Clinical course of one term. Ophthalmology alternates with dermatology as a special subject in the qualifying examination.

University of Lyons.

Clinical course of one term.

University of Montpellier.

No certificates required.

Switzerland.

The State examination for a diploma to practice medicine includes an oral and practical examination in ophthalmology conducted by two ophthalmic surgeons.

University of Basle.

A course of lectures during two terms and a clinical course of three terms.

University of Lausanne.

Clinical course of one term.

Spain.

Central University of Madrid.

Course of 82 lectures and clinical attendance from October to May. Examination at the end of the course conducted by the Professor of Ophthalmology.

University of Barcelona.

Course of 68 lectures; otherwise exactly as Madrid.

Sweden.

The examination in ophthalmology is entirely practical and oral, and is conducted by the Professor.

University of Upsala.

A course of lectures and two months' clinical course.

Norway.

Viva-voce examination as in Sweden.

University of Christiana.

Clinical course of one term.

Denmark.

University of Copenhagen.

Clinical course twice weekly during one term.

Occasional question in the surgery paper in the qualifying examination.

Japan.

University of Kyoto.

A course of lectures and a clinical course.

The examination in ophthalmology is oral and is conducted by ophthalmic surgeons.

The above analysis shows that Great Britain stands almost alone in granting diplomas to practice medicine without evidence of an adequate knowledge of diseases of the eye. There are still three examining bodies which have not even adopted the recommendation of the General Medical Council of 1891, which requires a certificate of attendance at a three months' clinical course. Moreover, at other institutions the interpretation of what is meant by a three months' course varies greatly and should be more accurately defined, as it is by all the American universities.

In Great Britain only a small minority of the licensing bodies apply regularly a test of ophthalmic knowledge. In Ireland and in the great majority of foreign universities, ophthalmology is one of the subjects of the qualifying examinations and the examiners are invariably ophthalmic surgeons.

NOTE.—*Since going to press we have received information as to the requirements of the Indian Universities of Bombay, Madras, and the Punjab (Lahore). In all three cases attendance at a course of systematic lectures, and of clinical instruction during a period of three months, is required. There is a special examination in Ophthalmology, consisting of a written paper and a practical and oral examination conducted by two ophthalmic surgeons.*

Part III.—The Need for Improved Instruction of Medical Students in Ophthalmology.

In the opinion of the Council the knowledge of ophthalmology possessed by the majority of medical students in Great Britain at the time of their qualification is inadequate to enable them to diagnose and treat efficiently cases of ordinary eye diseases met with in general practice. In 1917, Sir Arthur Downes in the "Report of the Departmental Committee of the Local Government Board on the Welfare of the Blind" (p. 60) quoted, and endorsed as still applicable, the statement made in the memorial presented by the Ophthalmological Society of the United Kingdom to the General Medical Council, in 1891, that "it is notorious that the general body of the profession does not possess a competent knowledge of diseases of the eye." Unless further action is taken in the matter this reproach to the medical profession will continue.

The Council hold that it is desirable that the training in ophthalmology should be mainly clinical, and they agree that a period of three months is all that can be allotted to the subject in a five years' curriculum. They, therefore, recommend: (1) that attendance at an ophthalmic clinic for not less than six hours a week during a period of three months shall be required of every student; (2) that such a period of clinical training shall be supplemented by a course of systematic lectures or clinical classes.

A very serious defect in the existing regulations is the absence of any test of the student's knowledge of ophthalmology in the qualifying examinations. Teachers in the medical schools are well aware that without the stimulus of an examination many students give the least possible attention to ophthalmology and may, and often do, finish their training without gaining even a rudimentary knowledge of the subject. In the opinion of the Council, it is most desirable that an examination in ophthalmology should be made an integral part of the qualifying examination by all those licensing bodies which have not hitherto included it in their schedule.

Internal Students.—When an examining board deals only with students trained within its own walls the system adopted by the universities of Edinburgh and St. Andrews has the

advantage of not adding to the burden of the qualifying examination. At the end of the course in ophthalmology there is a written and a practical examination, and certificates of admission to the qualifying examination are not granted to students unless they have attended the course regularly and have reached a definite standard in the class examinations.

The Council are of opinion that in such examinations, as in those for qualification, a second examiner should be associated with the teacher.

External Students.—A different problem confronts such examining boards as the universities of Oxford, Cambridge, and London, and the conjoint boards, which have to deal with students trained under diverse conditions in institutions over which the boards exercise little supervision. Such bodies should require definite evidence of regular attendance at an ophthalmic clinic and at a course of systematic instruction. In addition they should have a test that the student has acquired an adequate knowledge of the subject. The Council do not consider it essential that this test should be by a written examination, but they hold that there should always be a practical and oral examination in the diagnosis and treatment of the commoner diseases of the eye and in the use of the ophthalmoscope. Such an examination can only be carried out efficiently by ophthalmic surgeons who should also set and adjudicate on such ophthalmic questions as may be given in papers.

In the examination in ophthalmology, as in the examinations in pathology, surgical anatomy, etc., a candidate who does not attain to the required standard must be held to have failed to qualify in surgery.

Part IV.—Summary of Recommendations.

The Council therefore make the following recommendations:

(1) **No student shall be admitted to the final examination, qualifying to practice medicine, unless he has attended an ophthalmic clinic for not less than six hours a week during a period of three months, and has attended a course of systematic instruction in ophthalmology.**

(2) No student shall be considered to have passed the qualifying examination unless he has shown a sound knowledge of practical ophthalmology in an examination conducted by ophthalmic surgeons.

REPORT OF THE ANNUAL CONGRESS OF THE OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM.

By Mr. H. DICKINSON, London.

(*Concluded from the September number*)

THE BOWMAN LECTURE.

Plastic Operations on the Orbital Region.

Professor Morax delivered the Bowman Lecture, taking as his subject **plastic operations on the orbital region,** including **reflection of the orbital cavity, eyebrows, and eyelids.** The author opened with a felicitous acknowledgment in the name of France of the high honor conferred on him, and through him on French ophthalmology, by asking him to deliver this lecture. He said the prime motive for wishing to restore the appearance of the face when functional disability was not present was the avoidance of the unsettling curiosity manifested by the people met in the street, with which must be coupled the fear that his obvious defect would cause a lessening of affection on the part of those he held in esteem. There should be avoidance of the use of tissues in the formation of a flap in the regions of motor nerves, and the utmost degree of asepsis must be insisted on. He found the skin surface was sufficiently sterilized by sterilized soap and tincture of iodine: any organisms remaining were generally saprophytic. Hairy flaps sometimes harbored saprophytic organisms, and these might afterwards cause little foci of suppurating folliculitis. It was necessary to devise a method of securing more perfect sterilization of hairy flaps. When the conjunctival mucous membrane was alone at stake, one usually succeeded with physiological salt solutions, with instillations of zinc sulphate or silver nitrate. It was easier for the lacrimal mu-

cous membrane to be a source of infection. Some failures in this region had been due to operations having been done when there was latent dacryocystitis; and in such cases the extirpation of the lacrimal sac and its diverticula would alone be efficacious, the lacrimal canaliculi being excised. With regard to the destruction of eyebrows, by burning or the explosion of powder, when only one brow has been involved, it was easy to detach half its breadth, leaving a nasal pedicle, then fixing the isolated flap in an incision made symmetrically on a level with the upper margin of the orbit. When both eyebrows are destroyed, there must be recourse to non-pedicled hairy flaps, and these were less certain in results. He used for these cases flaps from the occipital region, fixing them in position by several mattress sutures. One disadvantage was that the hair on the new flap grew rapidly, and one of his cases had to have his eyebrow cut when he went to the barber's.

With regard to repairs to the eyelids, an extensive cutaneous destruction on a level with the lids was followed by an obvious modification of the palpebral fissure, and the mutilation would be even greater when it involved skin and subjacent tissues, muscle, etc. The first act in such cases must be to bring together the margins of the two lids, after having freshened the mucous margins in the usual way. In most cases, the union of the lids must be maintained for two or three months. Professor Morax entered into the technique in detail.

He proceeded to speak of repairs to the orbital cavity. When the wound received involved total or partial destruction of the eyeball and its mucous membrane, there was a shrinking scar of the orbit, and more or less complete adherence of the lid tissue to the orbital tissue, and these symblephara prevented the wearing of an artificial eye. Sometimes enucleation had been done by a surgeon who did not appreciate the importance of conserving every bit of mucous membrane. One must wait until the process of scar formation had been consolidated and there were no more signs of infection, before attempting to graft. Whenever possible, one had recourse to cutaneous pedicle flaps taken from the neighborhood. He described various types of case, and the procedures adopted.

With regard to complete symblepharon, if all the mucous

membrane was destroyed, the method described would have to be modified. He had found it best to openly expose the parts to be grafted, and keep them open until the graft was in good condition. In some cases it might be necessary to combine the dermo-epidermic grafting method with the pedicled flap one in total symblepharon. Professor Morax concluded by describing his methods of securing a mobile support for an artificial eye.

Eyesight and Education.

On Friday morning, at the Royal Society of Medicine, an interesting discussion took place on the subject of **eyesight in connection with education.** It was opened by Dr. JAMES KERR who said that at the present time any examination of the relations between vision and education rested much on the testing for acuity at school, while such matters as fatigue, functional troubles, the ocular results of various kinds of work, and the risks of visual deterioration were scarcely noted by those having the oversight of education. The use of the Ives grating and testing each eye separately did not yield fair results: the second tested eye usually gave the worst record, and he had now abandoned the method. He much preferred the copying of test types by children using both eyes, as this gave practically all the results required, and there was no waste of time. The results also provided a good basis for mass investigations. The tables in the earlier Board of Education Reports showed a great variation according to the districts concerned: *e. g.*, 19.5% with bad vision in Newcastle to 4.4% at Ashton-under-Lyne; 11.3% Lancashire, 4.8% Gloucestershire. By careful testing of very young children with test types, Dr. Margaret Hogarth got 86% normal vision in 800 infants, and only 3.2% cases of bad vision; she took every precaution to keep the attention fixed, and introduced a number of refinements. The local variations involved national problems, and were due, no doubt, largely to preventible causes, but there had not been any investigation on the question. He considered they were closely related to the general surroundings and were closely connected with the general health. The results in eye testing were largely influenced by the condition of the general cerebral cortex. Fatigue was important in academic work, and ocular

fatigue, though masked by great accommodative range in the young, was a contributor to nerve fatigue. With regard to myopia, four fifths of the children passed through all the strains and troubles of school life ocularly unharmed, but the majority who suffered from it became myopic. The increase of myopia year by year of age was not correlated to education, but to age. In a large number of cases Inglis Pollock showed that up to the fourteenth year 7% to 8% were myopic, but after that age it jumped to 15% to 19%, and remained above that figure. About puberty there was a real increase in the myopia present, also during the convalescence following acute illness. Sweden, by adopting classical education and Gothic print, had greatly increased the proportion of good vision in the country. He proceeded to emphasize the great importance in this connection of general nutrition. There should be careful measures to avoid glare and strong light contrasts, and children should be spared all unnecessary fatigue. He indicated the lines along which he thought further investigation should be carried.

Mr. N. Bishop Harman dealt with the clinical aspect of the subject, and he left out of account children who had attained to some stability of tissue and whose vision was good according to accepted standards. The remainder of the school population included (1) the immature; (2) the defective; (3) the blind.

With regard to class (1) the instability of accommodation and of binocular vision in early years was notorious, and this instability must extend to other functions. Owing to the intimate relation of brain and eye, the effect of any form of close work on the child was serious; to them, even the recognition of figures and letters was a mental feat, and he believed the eyes felt fatigued according to the degree of mental exertion. Adults had only to remember the ease with which they could skim over a novel for hours, yet felt fatigued by a comparatively short study of a scientific treatise. Yet the daily routine of the school child was comparable to the latter. When one read of the average work required of the average infant, one was led to inquire what was the average infant, but there was, as yet, no answer. No steps were taken to ascertain what the eyes of any particular infant were like nor whether its defects

would render the child incapable of bearing up against the strain put upon them. Between the fourth and seventh years the infant went through a training at school without any medical eyesight examination. The refraction could always be measured. He had examined the refraction of all the infants in a high-grade school in the west of London. The eyes of each child were anointed with a fresh preparation of homatropine and cocaine in castor oil (2% of each), then the child was allowed to sleep for an hour. After the examination the eyes were anointed with a minute smear of 1% eserine in oil, to effect closure of the pupils as quickly as possible. Three hundred and sixty-eight children, of ages four to seven, were examined; only eight wore glasses. Only eight had emmetropic eyes, but there were 232 hypermetropes, viz., 130 under 1 D., seventy-three under 2 D., while those with not more than 3 D. were twenty-nine. There were thirty-eight who had more than 2 D. astigmatism. Only very few had myopia of any degree, though one child had 18 D. Seven had scarred eyes, twenty-three had anisometropia of over 1 D., while eight had squint. The summary of his conclusions was, that one in every three was not fit to do ordinary school work under ordinary conditions, results which were striking and unexpected. He strongly condemned the practice of submitting young infants to school work without a preliminary examination of their eyes. There should be a definite grading of the little ones at these early ages. Indeed, the subject was sufficiently serious to warrant its examination by a committee of this society. He concluded by a description of special methods, such as those seen by members at their visit that day to the schools at Camden Town and Hampstead Road.

The subject was discussed by Mr. HARRISON BUTLER, Mr. ERNEST CLARKE, Mr. PERCIVAL HAY, Mr. A. L. WHITEHEAD, Mr. INGLIS POLLOCK, Mr. EVANS, Mr. G. W. THOMPSON, and the openers replied.

On Friday evening a series of papers were read and discussed.

Mr. TREACHER COLLINS and Mr. LESLIE PATON contributed a paper on **angioma of the choroid.** The patient, a boy, first came under Mr. Paton's care in 1917, when he was fourteen years of age. There was a large nævus on the left cheek and outer side of left orbit. There was detachment of retina out-

wards and downwards. The tension of the eye was then normal. Puncture of the sclera was made with the galvanocautery, but the vision did not improve. A year later, an acute attack of glaucoma occurred, and the eye was removed. There was found to be a lens-shaped mass in the choroid, measuring 9*mm* in length, 4*mm* in breadth, extending from the upper margin of the optic disk to a little behind the equator. There were the typical appearances of cavernous angioma. In the partitions between the vascular spaces on its inner surface were well developed lamellæ of bone.

Mr. ERNEST CLARKE read a paper on **presbyopia**, a subject, which, in the author's opinion, had been very inefficiently treated in the past in the various textbooks. Presbyopia synchronized with important body changes. The "squeezability" of the lens decreased with age, and in the normal emmetrope, at forty-eight years of age, it had decreased to such an extent that the person was conscious of requiring aid for near work. This was not a disease, but a physiological change, which affected all eyes alike. He considered that true presbyopia was entirely dependent on the lens, not due to any weakness of ciliary muscle, except in advanced age. Presbyopia was felt most at the time when eye-strain was most liable to occur, and Leonard Williams and others had shown the dangers of hypothyroidism, especially in connection with intestinal poisoning, for when the thyroid gland was deficient, the gate was opened for the poisoning of the system by toxines. He advocated the wearing of bi-focal glasses; a mistake commonly made in these was to give a too strong reading addition to them.

Colonel LISTER and Captain M. L. HINE contributed a paper on the condition of **evulsion of the optic nerve.** The authors had been able to find records of only twenty-two cases, and only four with a pathological report, yet during the war this condition of the optic disk had become familiar. It was recognized either by a hole at the optic disk, which might occupy the whole or a part of the scleral ring, or the disk might be filled apparently with white. In both cases the retinal vessels had either completely or partially disappeared. The tearing of the tissue resulted in gross hemorrhage at the back of the eye, so as to obscure the field for the ophthalmoscopic examination. When, as occasionally happened, little or no

hemorrhage took place into the vitreous, the ophthalmoscopic picture was one of the most striking possible: a fundus oculi without vessels, an optic disk replaced by an apparently bottomless glaucomatous pit set in a background in which there were dramatic concussion changes. The paper gave a minute description of the changes found, and was supplemented by a number of colored pictures, shown by means of the epidiascope.

Mr. E. HENDERSON read brief notes of a rare form of bilateral choroidoretinitis in a young child. The child, æt. six years, was brought on account of occasional convergent strabismus of the left eye. After wearing correcting glasses and having the defective eye trained, the strabismus disappeared. Two and a half years later, the sight having deteriorated, there was found in the right eye, a brilliant white exudation to the macular side of the disk, in the center of which was a circular, partly pigmented patch. Some months later the left eye suddenly failed. A similar symmetrical patch was found in the fundus, but accompanied by widespread exudation, and surrounded by some hemorrhage. No source of infection could be found, and the Wassermann and tuberculin tests were negative. The scattered exudation gradually disappeared, and the appearance at present closely resembled that of the fundus of the other eye. He regarded the condition as due to some unexplained choroidal vascular lesion.

The following papers were also read:

Mr. ARNOLD LAWSON, (1) **a new method of applying radium in diseases of the eye** (in collaboration with Mr. Sidney Russ who described the rationale). (2) **Flavine in ophthalmic surgery.**

Saturday morning was devoted to a clinical meeting at the Central London Ophthalmic Hospital, when many cases of interest were exhibited and discussed.

During the Congress, members visited the Day School for the Blind, Brecknock Road, Camden Town, the Myopia School, Exmouth Street, N. W., and the Wellcome Museum, Wigmore Street. A dinner was held at the Welbeck Palace Hotel, and a museum of exhibits and specimens was established, under the care of Mr. R. R. James. On Saturday afternoon many members gladly participated in a golf match at Northwood.

BOOK NOTICE.

VII.—**Manual of Neuro-Surgery.**

Prepared under the direction of the Division of Surgery in collaboration with the Section of Head Surgery, General Surgery, Orthopedic Surgery, and Neuro-Psychiatry, the Army Neuro-Surgical Laboratories, and the Instruction Laboratory of the Army Medical Museum; under the Supervision of the Surgeon-General. Washington: Government Printing Office, 1919. Distribution limited to the officers in the Medical Corps of the Army and to libraries receiving government literature.

This is an octavo volume of 492 pages, written by thirty-one contributors. Most of the ophthalmological portion was published in THESE ARCHIVES, vol. xlvii., No. 3, 1918, with the title "The Eye in Nervous Disease," by Ward A. Holden.

The book as a whole is a concise and well-illustrated treatise dealing first with the anatomy and physiology and then continuing with the diseases and injuries of the nervous system, with special attention given to surgical treatment. Considerable space is devoted to the relation of the eye, the ear, and the nasal sinuses to nervous affections, and the ophthalmologist will find the volume a lucidly written, happily condensed, and thoroughly practical work of reference on Neurology.

W. A. H.

INDEX OF AUTHORS AND SUBJECTS.

VOL. XLVIII.

Abducens Nerve, Variation in Distribution of the, in Man, (T. B. Magath) 67
Accidents, Injuries, and Parasites, 201, 413
Accommodation, Paresis of, (J. Wolff) 369
ALLING, A. N., Fat Transplantation into Tenon's Capsule after enucleation, 263
ANDREWS, JOSEPH A., Simple Electrical Device for Illuminating the Field of Operation in Operations on Eye, Nose, and Throat, 65
Angioid Streaks, (E. Brewerton) 378
Angioneurotic Œdema, (G. H. Bell) 522
Aniridia, Traumatic, Following Magnet Extraction, (H. H. Tyson) 283
Anterior Chamber, Eyelash in the, (E. M. Blake) 526
Antidiphtheritic Serum in Severe Ocular Infections with Special Reference to Hypopyon Keratitis, (Ben Witt Key) 581
Anti-Typhoid Vaccine, Keratitis Profunda Following Inoculation with, (G. H. Bell) 273, 368
Argyrosis of Conjunctiva and Cornea, (J. E. Weeks) 527
Artificial Eyes in Operations Substituted for Enucleation, (P. Gougelmann) 268
Aviators, Further Experience in the Ocular Functions of, (W. H. Wilmer) 439
Aviators, Visual Requirements of, Discussion on, 519

BELL, GEORGE HUSTON, Keratitis Profunda in both Eyes, Following Inoculation with Anti-Typhoid Vaccine, 273
BELL, GEORGE, and TOUSEY, SINCLAIR, Non-Operable Tumor of the Orbit and Brow Treated Successfully with Radium. Report of a Case, with Remarks, 531
Blood Pressure in Retinal Arteries, (Baillart) 181
Book Reviews, 203, 632
BUTLER, T. HARRISON, Acute Retrobulbar Neuritis in a Baby, 240; Plastic Surgery of the Eyelids after War Injuries, 103

CALHOUN, F. PHINIZY, Ocular Complications Due to Typhoid Inoculations, 553
Cataract, Cholesterine Crystals in Hypermature, (J. E. Weeks) 527; Glaucoma Following Spontaneous Absorption of, (H. Gifford) 196; Secondary Following Extraction of a Dislocated (Traumatic) Lens, (W. H. Wootton) 286
CHARLES, J. W., A Positive Focal Tuberculin Reaction in a Spindle-Cell Sarcoma, which had Perforated the Sclera, 568
Choroid, Angioma of the, (Collins and Paton) 629; Conglomerate Tubercle of the, (C. W. Cutler) 300; Reports on the, 194; Subretinal Exudate Simulating Sarcoma of the Choroid with Anatomic Examination, (Arnold Knapp) 559; Tuberculosis of the, (A. E. Davis) 525
Ciliary Region, Sarcoma of the, (E. Tôrôk) 294
CLARK, C. F., Coloboma and So-

CLARK, C. F.,—*Continued*
called Congenital Dislocation of the Lens, 475
COBB, PERCY W., A Contribution to the Study of Dark-Adaptation, 492
COHEN, MARTIN, A Device for Examination of Distant Stereoscopic Vision for Form and Colors, 142, 168; Primary Intradural Tumor in the Orbital Portion of the Optic Nerve, 19
Coloboma and So-called Congenital Dislocation of the Lens, (C. F. Clark) 475
Conjugate Deviation of the Eyes with Astereognosis, (H. A. Riley) 340
Conjunctiva, Reports on the, 189, 404; Tuberculosis of the, (M. Cohen) 96
CONNELLAN, J. G., Treatment of Intestinal Infections, 350, 527
Cornea, Appearances of the, after Inflammation, (Holmes Spicer) 99; Congenital Pigmentation of the, (R. Ford) 379; Reports on the, 191, 405
Cystotome Manœuvre, Extraction of Mature and Immature Cataractous Lenses within the Capsule, (J. A. Kearney) 62

Dark-Adaptation, Study of, (P. W. Cobb) 492
DERBY, G. S., Eye Work with the British Expeditionary Forces in France, 217
DICKINSON, H., Report of the Annual Congress of the Ophthalmological Society of the United Kingdom, 516, 625
Distance, Judgment of, with Semaphores and a Screen at 100 Meters, (H. J. Howard) 461
Distance Stereoscope, (Cohen) 142, 168; James's, (H. J. Howard) 168
DOLMAN, PERE, The Maddox Rod Test, 503
DUANE, A., The Basic Principle of the Diagnosis in Motor Anomalies of the Eyes, 1
DUNN, JOHN, Note on Surgery of Meibomian Cysts, 43; The Pupil in Glaucoma, 126
DWYER, J. G., Further Reports of Focal Infections of the Eye from Intestinal Tract, 344, 527

Encephalitis Lethargica, Cases of, (H. Woods) 536
Epiphora, Radical Treatment of, (A. Wiener) 334
Excision of the Eye, Substitute Operations for, Papers on, 267; Discussion, 291
Exophthalmos, Spontaneous Pulsating, (H. H. Tyson) 523; Traumatic Pulsating, (G. H. Bell) 84
Eye, The, in Relation to General Diseases, Reports on, 177, 394
Eyeball and Lids, Epithelioma of the. Operation. No Return after Six Years, (Dunbar Roy) 563
Eyelid, Horn of the, (G. H. Bell) 523
Eyelids, Autogenous One-Piece Epithelial Grafts for Restoration of the, (E. B. Heckel) 311; Plastic Surgery of the, after War Injuries, (T. Harrison Butler) 103; Reports on the, 187, 401
Eyes, Surgery after War Injuries of the, (G. H. Grout) 227
Eyesight and Education, (James Kerr) 606

Fat Transplantation into Tenon's Capsule after Enucleation, (A. N. Alling) 263
Fat Implantations, (B. W. Key) 292
Foreign Body in Globe of Eye, (W. E. Lambert) 284
Foreign Body, Retinal Degeneration from, (A. C. Hudson) 304

Glass Ball Implantation into Tenon's Capsule, (H. J. Howard) 263
Glaucoma, Double Sclerotomy in, (G. Young) 518; Future Operation for, (Herbert) 518; Spontaneous Reduction of Tension in, (A. Knapp) 525; The Pupil in, (John Dunn) 126
Glaucoma and Intraocular Tension, Reports on, 196, 409
Glioma, Radium Treatment of, (Schoenberg) 485, 522
Gold in an Eye, (G. H. Bell) 93
GOUGELMANN, PIERRE, Substitute Operations for Enucleation, from the Standpoint of the Maker of Artificial Eyes, 268
GROUT, GERALD H., Experiences in Reparative Surgery after War Injuries of the Eyes, 227

HECKEL, EDWARD B., Autogenous One-Piece Epithelial Grafts for Restoration of the Eyelids, 311

Herpes Zoster, Retrobulbar Neuritis and Acute Glaucoma, Following, (C. A. Veasey) 364
HOLMES, CHRISTIAN R., Extirpation of Lacrimal Gland for Epiphora, 323, 374
HOWARD, HARVEY J., Implantation of a Glass Ball within Tenon's Capsule by Verhoeff's Method, 265; Judgment of Distance with Semaphores, and a Screen at 100 Meters, 462
Hyaloid Artery, Case of Persistent, (J. M. Wheeler) 87

Illuminating Device, A Simple Electrical, for Illuminating Field of Operations on Eye, Nose, and Throat, (J. A. Andrews) 65
Instruments and Remedies, Reports on, 180, 397
Interstitial Keratitis, (McDannald) 523
Intestinal Infections, Treatment of, (J. J. Connellan) 350; (Dwyer) 344, 527
Intraocular Growth, (Carruthers) 379
Intraocular Pressure and Tonometry, Experimental Studies in, (W. McLean) 23
Iridocyclitis from the Teeth, (G. H. Bell) 85
Iris, Atrophy of the (Feingold) 192; Reports on the, 192, 406
Iris and Ciliary Body, Sarcoma of the, (E. M. Alger) 372

Jaw-Winking Phenomenon, Explanation of, (Anton Lutz) 144

KEARNEY, J. A., Cystotome Manœuvre, Extraction of Mature and Immature Cataracts within the Capsule, 62
Keratitis Nodulosa, (G. H. Bell) 92
Keratitis Profunda, (or Disciformis?) (F. H. Verhoeff) 449
Keratitis Striata, (M. Cohen) 95
KEY, BEN WITT, Antidiphtheritic Serum in Severe Ocular Infections with Special Reference to Hypopyon Keratitis, 581
KNAPP, ARNOLD, Report of a Carcinoma of the Orbit, 120; Sub-Retinal Exudate Simulating Sarcoma of Choroid, with Anatomic Examination, 559; The Autotoxic Factor in Sympathetic Ophthalmia, 356

Laboratory, A Medical Research; with Special Reference to Ophthalmology, (W. B. Lancaster) 287
Lacrimal Gland, Extirpation of, for Relief of Epiphora, (C. R. Holmes) 323; Primary Nocardiasis of the, (J. B. Christopherson and R. C. Archibald) 100; Sarcoma of the, (E. M. Alger) 372
LAGRANGE, FELIX, "Atlas d' Ophtalmoscopie de Guerre" Review of, 212; "Fractures of the Orbit and Injuries of the Eyes in War," Notice of, 210
LANE, FRANCIS, Persistent Posterior Fibrovascular Sheath of the Lens. Report of Two Clinical Cases, and Three Eyeballs Examined Microscopically, 572
Lens, Persistent Posterior Fibrovascular Sheath of the; Two Clinical Cases of, and Microscopical Examination of Three Eyeballs, (Francis Lane) 572; Removal of Dislocated, by Electric Illumination, (H. S. Paine) 193; Reports on the 193, 407
Lenses, Congenital Dislocation of both, (W. E. Lambert) 84; (C. H. Schlichter) 294; (J. R. Shannon) 162; Double Dislocation of, (A. Knapp) 284
Leprosy of Brow and Cornea, Maculo-Anæsthetic, (J. E. Weeks) 527
Lids, Restoration of the, with Wolff's Graft, (R. G. Reese) 162
Literature, General Ophthalmological Reports on, 175, 391
LLOYD, RALPH I., Phantom Intraocular Tumor, Multilocular Cyst of Iris, and Ciliary Body, 489
LUTZ, ANTON, The Jaw-Winking Phenomenon and its Explanation, 144

Macula, Congenital Coloboma of the, (S. A. Agatson) 377
Maculæ, Disease of Both, (R. Batten) 379
Macular Region, Tumor of the, (A. J. Wiesner) 371
Maddox Rod, Tests with, (P. Dolman) 503
MAGATH, THOMAS BYRD, A Variation in the Distribution of the Nervous Abducens in Man, 67

Magnet Extraction, Traumatic Aniridia Following, (H. H. Tyson) 283
Malingerers, Instrument for Detection of, (Ellice M. Alger) 166
"Manual of Neuro-Surgery." Book Notice, 632
McLEAN, WILLIAM, Experimental Studies in Intraocular Pressure and Tonometry, 23
Meibomian Cysts, Note on Surgery of the, (J. Dunn), 43
Migraine, (J. Herbert Fisher) 384
Miscellaneous Notes, 530
Motor Anomalies, Basic Principle in Diagnosis of the Eye, (A. Duane) 1
Motor Apparatus of the Eye, Reports on, 185, 400
Mules, Operation, (J. E. Weeks) 291

Negroes, Eyesight of the, in Africa, (J. N. Roy) 72
Neuritis, Acute Retrobulbar, in a Baby, (T. H. Butler) 240; Case of Retrobulbar in a Child with Intestinal Stasis, (M. J. Schoenberg) 56
New York Academy of Medicine, Report of Proceedings of the Section on Ophthalmology of, 84, 162, 283, 368, 522

Observations on Eye Work with the British Expeditionary Forces in France, (G. S. Derby) 217
Ophthalmological Society of the United Kingdom, Program of Annual Congress, 159; Report of the Annual Congress of the, 516, 625
Ophthalmologists, Council of British. Report on the Teaching and Examination of Medical Students in Ophthalmology, 614
Ophthalmology, Reports on the Progress of, 175, 391
Report on the Teaching and Examination of Medical Students in Ophthalmology, (Council of British Ophthalmologists) 614
Ophthalmoplegia Interna, Following Pneumococcic Conjunctivitis, (S. A. Agatston) 369
Optic Atrophy and Sella Turcica Degeneration, (J. Taylor) 306
Optic Nerve, Evulsion of the, (Lister, and M. L. Hine) 630; Primary Intradural Tumor of Orbital Portion of the, (M. Cohen) 19; Reports on the, 200, 403
Orbit, Extraordinary Case of Foreign Body, in the, (E. S. Sherman) 286; Ivory Exostosis of, (Armour and Lang) 305; Pulsating Tumor of the, (R. Ford) 379; Report of Carcinoma of the, (Arnold Knapp) 120; Revolver Bullet Injury of the, with Eye Symptoms, (J. A. Spalding) 317; Tumor of the, (R. G. Reese) 169
Orbit and Accessory Cavities, Inflammatory Diseases and Injuries Affecting the, Discussion on, 384
Orbit and Brow, Report of a Case of Non-Operable Tumor of the, Successfully Treated with Radium, (G. H. Bell, and Sinclair Tousey) 531
Orbital Abscess, (J. Wolff) 370
Orbital Region, Plastic Operations on the, (Morax) 625
Orbital Tumor, (Hough, P. B.) 526; (E. S. Thomson) 373
Orbits, Accessory Sinuses, Exophthalmos, Reports on, 188, 402
Oxford Ophthalmological Congress, Reports on, 309

Panophthalmia, Experimental Production of by Infection from the Blood Stream, (P. Wegeforth) 276
Paralysis of Associated Movements from Syphilis, (M. J. Schoenberg) 86
Phantom Intraocular Tumor, Multilocular Cyst of Iris and Ciliary Body, (R. I. Lloyd) 489
Pathology and Bacteriology, Reports on, 179, 397
Pituitary Region, Tumor in the, (K. Schlivek) 289
Pituitary Struma, (H. H. Tyson) 368
Pituitary Tumors, (Cargill) 380; (R. Ford) 379; (Maxted) 381; (Ormond) 380
Poisons, Reports on, 183
POSEY, WM. CAMPBELL, Review of "Hygiene of the Eye," 207
Ptosis, Double Congenital, (A. E. Davis) 525

Radium and Flavine in Eye Diseases, (Lawson and Russ), 631

Radium Treatment, Cases of Success from, 531
Refraction and Accommodation, Reports on, 184, 399
Retina, Angioma of the, (E. Brewerton) 306; Bilateral Glioma of, Apparently Arrested in the Non-Enucleated Eye by Radium, (M. J. Schoenberg) 485; Dilatation of Vessels in the, (H. Goldsmith) 100; Quiescent Foreign Body in the, of Five Months' Standing, (Arnold Knapp) 166
Retina and Vitreous, Reports on the, 198, 412
Retinitis Pigmentosa, (Treacher Collins) 517
Retinitis Proliferans, (M. Schlivek) 86
Retinitis Punctata Albescens, (S. A. Agatston) 294
RILEY, HENRY ALSOP, Report of a Case of Conjugate Deviation of the Eyes, with Hemiastereognosis, 340, 371
ROY, DUNBAR, Two Cases of Epithelioma of the Eyeball, and Lids. Operation. No Return after Six Years, 563
ROY, J. N., The Eyesight of the Negroes of Africa, 72
Royal Society of Medicine, Reports of Transactions of the Ophthalmological Section of the, 99, 304, 378

Sarcoma, Positive Focal Tuberculin Reaction in a, which had Perforated the Sclera, (J. W. Charles) 568
SCHOENBERG, MARK J., A Case of Acute Retrobulbar Neuritis in a Child, with Intestinal Stasis (Congenital Dilatation of the Colon) 56; Case of Bilateral Glioma of Retina, Apparently Arrested in the Non-Enucleated Eye, by the Radium Treatment, 485, 522
DE SCHWEINITZ, G. E., Concerning the Ocular Phenomena in the Psychoneuroses of Warfare, 419
Sclera, Anterior Ectasia of, (A. Knapp) 97
Scotomata, Two Instances of Scintillating, Rarely Described, (J. A. Spalding) 38
SLUDER, GREENFIELD, "Concerning Some Headaches and Eye Disorders of Nasal Origin," Review of, 208
SNELL, ALBERT C., Injuries of the Superior Oblique Muscle, Report of a Case, 111
SPALDING, J. A., Revolver Bullet Injury of Both Orbits, with Ocular Symptoms, 317; Two Instances of Scintillating Scotomata Rarely Described, 38
Stereoscopic Vision, A Device for the Examination of, for Form and Colors, (Martin Cohen) 142
Sub-Retinal Exudate, Simulating Sarcoma of Choroid, with Anatomical Examination, (Arnold Knapp) 571; Sub-Retinal Exudate, (L. W. Crigler) 165
Superior Oblique Muscle, Injuries of the, with Report of a Case, (A. C. Snell) 111
SWEET, WILLIAM M., Implantation of Metal Ball in Tenon's Capsule, 257
Sympathetic Ophthalmia, Reports on, 194, 409; The Autotoxic Factor in, (A. Knapp) 356
Sympathetic Ophthalmitis with Fundus Changes, (F. Moore) 307

TAYLOR, ROBERT HENRY, "Glaucoma," Review of, 203
Teeth, Influence of, on the Eye, Discussion of, 85
Tenon's Capsule, Implantation of Metal Ball in, (W. M. Sweet) 257; Various Implantations Into, 257
Test Types, British Report on Standard Illumination of, 170
Tonometry, Discussion on, 88
TÖRÖK, ERVIN, Tuberculin in Diagnosis and Treatment of Eye Diseases, 242
TOUSEY, SINCLAIR, and GEORGE HUSTON BELL, Non-Operable Tumor of the Orbit and Brow, Treated Successfully with Radium. Report of a Case with Remarks, 531
Trachoma with Heisrath-Kuhnt Operation, (L. W. Crigler) 93
Treatment and Diagnosis, Reports on, 181, 398
Trephining, Late Infection Following, for Buphthalmos, (L. W. Crigler) 165
Tuberculin in Treatment and Diagnosis of Eye Diseases, (Ervin Török) 242, 295
Tubercular Endovasculitis, in Retina, (M. Uribe-Troncoso) 89

Typhoid Inoculations, Ocular Complications Due to, (F. Phinizy Calhoun) 553

VALOIS, G., "Les Borgnes de la Guerre," (The One-Eyed in War), Review of, 213
VEASEY, CLARENCE A., Report of Unusual Complications (Retrobulbar Neuritis and Acute Glaucoma) of Herpes Zoster Ophthalmicus, 364
VERHOEFF, F. H., A Case of Keratitis Profunda (or Disciformis) with Microscopical Examination, 449
Visual Field, Homonymous Quadrant Defects of the, (J. E. Weeks) 163

War, Ocular Phenomena in the Psychoneuroses of, (de Schweinitz) 419; The Eyes in, (Duverger) 176
WEGEFORTH, PAUL, Experimental Production of Panophthalmia, by Infection from the Blood Stream, 276
WIENER, A., Radical Treatment of Epiphora, 334
WILMER, W. H., Further Experience in the Ocular Functions of Aviators, 439
WOODS, HIRAM, Some Cases of Lethargic Encephalitis, 536

TO
GREATER VISION THROUGH
OPTICAL SCIENCE
BAUSCH
& LOMB
THROUGH · CLASS · MAKING · AND · SCIENTIFIC · COMPUTATION · TO · FINISHED · PRODUCT ·

BAUSCH & LOMB OPTICAL COMPANY

Rochester, N. Y.

New York Washington Chicago San Francisco London

Makers of Ophthalmic Lenses and Instruments, Microscopes, Photographic Lenses, Balopticons, Binoculars, Magnifiers, Readers, and other High-Grade Optical Products

Artificial Human Eyes Made to Order

Prof. Snellen Reform Eyes a Specialty

We are specialists in the art of making artificial eyes. We have supplied the leading Eye Infirmaries since our establishment in 1853, and the quality of our work is indorsed by the leading oculists.

Charitable Institutions are Supplied at Lowest Rates

We have a large stock of shell and reform eyes constantly on hand. Selections sent, and special discounts to oculists. Send for order blank.

104 East 12th St. MAGER & GOUGELMANN New York

Gall & Lembke

Practical and Manufacturing Opticians

5 West Forty-Second Street, N. Y.

TRIAL CASES OPHTHALMOMETERS

PHOROMETERS PERIMETERS

OPHTHALMOSCOPES TEST TYPES

TRIAL FRAMES PRISM SETS

RETINOSCOPES SKIASCOPIC EYE MODELS

CLINOMETERS

Established 1842

THE
DR. SNELLEN
FULL BACK
REFORM EYE

ARTIFICIAL HUMAN EYES

Eyes made to order and satisfaction guaranteed in the most difficult cases

We also carry a large stock of Snellen Full Back Reform Eyes, also of the regular shell eyes.

We will make special low prices to charitable institutions.

Correspondence invited

as we are desirous of proving the superiority of our product

Write for our Booklet F on Snellen Eyes

Charles Fried 36 East 23d St., Near 4th Ave. NEW YORK

School of Ophthalmology

Instruction in Ophthalmology is given at the HERMAN KNAPP MEMORIAL EYE HOSPITAL, 57th Street and 10th Avenue, in (*a*) a systematic course covering all branches, beginning October and February; and in (*b*) short practical courses on External Diseases, Refraction, Ophthalmoscopy, Operative Surgery, Pathology, and Physiological Optics. For particulars apply to Dr. Arnold Knapp, at the Hospital, 500 West 57th Street, New York City.

Engraving and Stationery

A large number of people who reside at a distance from the principal cities, not understanding the facility and accuracy with which orders for Engraving and Stationery can be filled through the mails, are obliged to content themselves with a very inferior grade of Stationery, and of Engraving and Printing, when, by sending their orders to headquarters, they can have the same executed at moderate prices and in a thoroughly artistic manner. In the extensive Stationery Department of Messrs. G. P. PUTNAM'S SONS, Original Designs for Monograms, Crests, and Coats-of-Arms are furnished for stamping on note and letter paper. Visiting Cards, Wedding and Reception Invitations are engraved and printed in the correct style, while their exceptional facilities enable Messrs. PUTNAM to execute all such work at the lowest prices that are consistent with a high standard of excellence.

Their stock of Fine Writing Papers is extensive, and contains all the latest novelties, many of the same being specialties manufactured exclusively for their Retail Department. Messrs. PUTNAM are now conducting an extensive trade through the mails, and are in a position to supply the wants of their customers promptly, intelligently, and economically. They furnish estimates and samples for every description of engraving and printing.

G. P. Putnam's Sons

2, 4, and 6 West 45th St., New York 24 Bedford St., Strand, London